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INVITED MEDICAL REVIEW

Emerging and changing viral diseases in the new millennium

C Scully[1,2], LP Samaranayake[3]

[1]*WHO Collaborating Centre for Oral Health-General Health, London;* [2]*UCL, London, UK;* [3]*Oral Microbiomics and Infection, School of Dentistry, University of Queensland, Brisbane, Qld, Australia*

Most viral infections encountered in resource-rich countries are relatively trivial and transient with perhaps fever, malaise, myalgia, rash (exanthema) and sometimes mucosal manifestations (enanthema), including oral in some. However, the apparent benignity may be illusory as some viral infections have unexpected consequences – such as the oncogenicity of some herpesviruses and human papillomaviruses. Infections are transmitted from various human or animal vectors, especially by close proximity, and the increasing movements of peoples across the globe, mean that infections hitherto confined largely to the tropics now appear worldwide. Global warming also increases the range of movement of vectors such as mosquitoes. Thus recent decades have seen a most dramatic change with the emergence globally also of new viral infections – notably human immunodeficiency viruses (HIV) – and the appearance of some other dangerous and sometimes lethal infections formerly seen mainly in, and reported from, resource-poor areas especially in parts of Asia, Latin America and Africa. This study offers a brief update of the most salient new aspects of the important viral infections, especially those with known orofacial manifestations or other implications for oral health care.

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Introduction

Professor Jens Pindborg, in a lecture in the 1970s, spoke of the very few viral infections then known, most of which were regarded as relatively trivial, transient and with few or no serious sequelae and which were largely clinical phenomena with few therapies available (Scully, 1979). Indeed, most viral infections encountered in resource-rich countries were and still are, usually relatively trivial and transient with perhaps fever, malaise, myalgia, rash (exanthema) and sometimes mucosal manifestations – an enanthema, and these have been well documented (Scully and Samaranayake, 1992).

Gradually, however, the unexpected consequences of some oral viral infections have emerged and been recognised, not without some surprise (Scully, 1983) especially the oncogenicity of some herpesviruses (Eglin *et al*, 1983) and human papillomaviruses (HPVs) which we (Eglin *et al*, 1983; Maitland *et al*, 1987; Cox *et al*, 1993) and many others (e.g. Lind *et al*, 1986) have explored, culminating in the appreciation of unanticipated transmission routes for some cancers, such as sexual (Scully, 2002).

Viruses are increasingly appreciated to cause a wide range of human diseases, ranging from acute self-resolving conditions to acute or chronic fatal diseases. Effects that arise long after the primary infection can increase the propensity for chronic conditions (e.g. erythema multiforme) or in some, lead to the development of cancers other than oral (Herrington *et al*, 2015). In addition, other viruses such as hepatitis C virus (HCV) have been implicated in common but diverse oral lesions such as lichen planus/lichenoid lesions and sicca syndrome (Baccaglini *et al*, 2013), the latter also sometimes arising after some other viral infections (Youinou *et al*, 2005) although the full aetiopathogenesis of Sjogren syndrome remains unclear (Kivity *et al*, 2014). The possible viral associations in many other oral conditions including periodontitis (Vincent-Bugnas *et al*, 2013; Ambili *et al*, 2014; Contreras *et al*, 2014; Ly *et al*, 2014) and several conditions of unknown aetiology, however, remain enigmatic, and associations are not necessarily causal.

The recent several decades have also seen a most dramatic change with the emergence globally of new viral infections – notably human immunodeficiency viruses (HIV) – and the appearance also in resource-rich countries, of some other dangerous and sometimes lethal infections hitherto latent, unrecognised or unappreciated in resource-

Correspondence: Crispian Scully, CBE, FMedSci, DSc, FDS, WHO Collaborating Centre for Oral Health-General Health; and UCL, 256 Gray's Inn Road, London WC1X 8LD, UK. Tel: 020 7915 1038, Fax: 020 7915 1039, E-mail: Crispian.scully@ucl.ac.uk
Both authors have equally contributed to the review.
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poor areas. Rare lethal and other dangerous viral infections were formerly seen mainly in, and reported from, resource-poor areas of Asia, Latin America and Africa. Pandemics of severe acute respiratory syndrome (SARS) and influenza viruses (both H5N1 and H1N1), heralded the surge of zoonotic virus outbreaks. Laboratory diagnosis of viral infections is traditionally based on the isolation of the virus, detection of viral nucleic acid or antigens, or serological confirmation (generally presence of IgM antibodies), and it is clear that the rate of discovery of new viruses is accelerating, due to a combination of true emergence of new pathogens, increasing awareness and the advance of new mainly molecular biology technologies making rapid detection and characterisation possible (Wang, 2011). Various respiratory viruses and Ebola virus disease (EVD) in particular have served to awaken humanity to the related social inequalities and challenges.

This study discusses the importance of emergent new infections and recent findings in relation mainly to those viral infections that may manifest orally or may affect oral health care. Fuller descriptions of Ebola virus, Marburg virus, coronaviruses, Nipah virus, noroviruses, enteroviruses, HIV, measles, mumps, respiratory syncytial virus (RSV), influenza, cytomegalovirus (CMV), varicella zoster virus (VZV), Epstein–Barr virus (EBV), HPVs and Kaposi's sarcoma-associated herpesvirus (KSHV) are available elsewhere (e.g. Herrington *et al*, 2015).

Emergence of viral infections

It is increasingly evident that there is now an amazing range of viral agents, many unidentified, which may be new or newly recognised or old, re-emerging.

Risk factors for infection include more risk

- from greater exposure,
- if defences are down,
- if agents evade defences,
- generally in warm, moist places.

Emerging viral diseases have arisen mainly because of increasing and changing air travel habits, but other factors that have also increased exposure to the vectors of these infections include conflicts, displacement and migration, as well as changing climate and vector distribution, changing farming/manufacturing, changing lifestyles such as promiscuity and changing clinical practices (Mathis *et al*, 2015).

Transmission of respiratory and enteric viruses is high – while sexually shared infections (SSI) are of low infectivity – generally requiring the close apposition of infected mucosae, increased when there is epithelial discontinuity. However, with the existence of transnational sexual networks in many countries including USA (Hughes, 2001) and Europe, with high rates of migration and travel between, for example, Amsterdam, Barcelona, Berlin, London and Paris, there have been SSI outbreaks among sexually exploited people of both genders but especially in HIV-positive men. Such close encounters, as well as large gatherings of humans, and/or prolonged periods in confined spaces, can enhance transmission of many agents; this has led to the development of a new area of medicine – 'mass gathering medicine (MGM)' (Memish *et al*, 2012).

Mass gatherings consist of large numbers of people attending an event at a specific site for a finite time. Some of the largest mass gatherings are spiritual in nature but other examples include Olympics, rock concerts and political rallies. The public health issues associated with the Hajj (the annual Muslim pilgrimage to Mecca, Saudi Arabia) is the best reported and has international or even intercontinental implications in terms of infection spread. Hajj routinely attracts 2.5 million Muslims (Memish *et al*, 2012), and the unavoidable overcrowding raises the risk of respiratory infections. 'Hajj cough' is the most frequently reported but influenza (Shafi *et al*, 2008; Haworth *et al*, 2013) and bacterial meningococcal W135 strains16 are more serious – as are severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) coronaviruses – new viruses that cause severe acute lower respiratory infections (ARI), with 10% and 35% mortality rates, respectively, and >50% mortality rates seen in older and immunosuppressed people (Gralinski and Baric, 2015).

The past decade has also seen the emergence of several other novel viruses that have appeared in resource-rich countries – often in travelling people – including an H7N9 influenza A virus, a swine-like influenza H3N2 variant virus and a human adenovirus 14p1 (Gautret *et al*, 2014). A number of zoonotic and vector borne viral diseases have emerged in South-East Asia and the western Pacific including Japanese encephalitis, Barmah Forest and Ross River viruses. Australia sees Ross River and Barmah viruses now appearing regularly. Nipah virus causes limited but deadly epidemics in South-East Asia. Finally, infections by lyssa viruses, Kunjin, Murray Valley and Zika viruses are also emerging (Bhutta *et al*, 2014; Carson *et al*, 2015).

In USA, the Centers for Disease Control and Prevention (CDC) recognise such threats and have a MISSION CRITICAL (Frieden *et al*, 2015) which focuses on antibiotic resistance and viral infections as shown in Box 1.

Coronaviruses cause illnesses ranging from the common cold to SARS. MERS-CoV has an especially high mortality and has recently spread widely outside the Middle East to Asia. Dr Frieden, Director of CDC, had stated 'In this interconnected world we live in, we expected MERS-CoV to make its way to the United States. We have been preparing since 2012 for this possibility (Frieden *et al*, 2015)'.

Avian influenza A (H5N1) and A (H7N9) viruses have continued to circulate widely in some poultry populations and infect humans sporadically. Sporadic human cases of

Box 1: CDC mission critical infections

- Ebola
- EV D68 (enterovirus)
- HIV
- MERS (Middle East respiratory syndrome) coronavirus (CoV)
- Poliomyelitis virus.

avian A(H5N6), A(H10N8) and A(H6N1) have also emerged. Closure of live poultry markets in China has reduced the risk of A(H7N9) infection (Hui and Zumla, 2015).

Standard infection control precautions are mandatory to prevent cross-transmission from recognised and unrecognised sources of infection. These sources of (potential) infection include blood and other body fluid secretions or excretions (excluding sweat, non-intact skin or mucous membranes) and any equipment or items in the care environment which are likely to become contaminated (Booty *et al*, 2010).

Recognising new viral infections

RNA viruses, with their high potential for mutation and epidemic spread, are the most common new viral causes of human disease. Most emerging viruses are zoonoses; they have jumped from mammals or birds to humans. The annual rate at which novel viruses have been found remains at 2–3 a small number which is an artefact of inadequate surveillance in resource-poor countries, where even established endemic pathogens are often misdiagnosed. Indeed, many of the emerging viruses of the future are *already* infecting humans (Rosenberg, 2015).

More awareness, internet communications, advances in diagnostic technology [high-throughput sequencing and specific polymerase chain reaction (PCR) assays] now help assists recognition. ProMED-mail is one robust and sensitive mechanism for the discovery of emerging disease outbreaks and for rapid dissemination of information to the public health community (Madoff and Woodall, 2005). For example, severe fever with thrombocytopenia syndrome (SFTS) was recognised as associated with a novel SFTS bunyavirus (SFTSV) (Bao *et al*, 2011; Jiang *et al*, 2015) using real-time reverse transcription PCR (RT-PCR), viral culture, genetic sequencing, microneutralisation assay (MNA) and indirect immunofluorescence assay (IFA). Another example is a new arenavirus related to lymphocytic choriomeningitis viruses that was recognised in a cluster of fatal transplant-associated diseases (Palacios *et al*, 2008). Specific PCR assays showed the virus in the kidneys, liver, blood and cerebrospinal fluid of the transplant recipients.

Viral infections with some orofacial manifestations

Awareness of the infections possible and likely, their epidemiology, and a history of travel, contact and relevant vaccinations is crucial to diagnose an infection, but the history is often overlooked. Virus infections typically manifest with a fever, but this is neither always present nor measured by the clinician. Clinical features are often non-specific and may include malaise, myalgia, rashes and mucosal lesions such as ulceration or bleeding. These are not always major features, not always checked by a clinician, or may often be seen by non-orally trained healthcare workers. Examination conditions in the field may be less than ideal; thus, underdiagnoses or misdiagnoses are likely to be quite common.

Ebola virus disease

Although EVD has been recently discussed fully elsewhere (Samaranayake *et al*, 1996, 2015; Scully *et al*, 2014), we provide a brief overview account of its oral manifestations below.

The three cardinal oral signs and symptoms of EVD are gingival bleeding, mucosal lesions (see below) and pain (odynophagia). Other important features typical of early and mild forms of disease, which may help oral health care providers suspect EVD, include epistaxis, bleeding from injection sites, conjunctivitis and rash. Bleeding is very frequent in advanced forms of EVD, but it is only relatively frequent in mild or early EVD forms; thus, it is likely that Ebola-infected patients seeking care may not show such a sign. Typically, gingival bleeding is concomitant with other forms of bleeding, particularly epistaxis and bleeding from injection sites. Concurrent bleeding at disparate sites is a discriminatory sign of EVD.

Mucosal lesions such as white or red patches, aphthous-like ulceration and greyish exudative lesions may be seen in EVD, but these remain to be more accurately defined. Odynophagia (discomfort), the consequence of oedema and mucosal lesions, may range from sore throat to severe dysphagia, when mucosal lesions are ulcerated.

Ebola virus disease is readily transmitted by body fluids, so universal infection control is essential. There is no reliably effective antiviral against this agent yet available.

Dengue

Dengue viruses (DENVs) cause dengue – the most common arthropod-borne viral disease in humans – now seen in more than 100 tropical countries. The word dengue is obtained from Swahili phrase Ka-dinga pepo meaning 'cramp-like seizure'. It is also called break-bone fever.

Dengue virus infection can be asymptomatic or a self-limited, acute febrile disease ranging in severity. The classical form is characterised by high fever, headache, abdominal pain, morbilliform rash, myalgia and arthralgia. In a small proportion of cases, the disease progresses to life-threatening dengue haemorrhagic fever, which results in non-infectious bleeding, thrombocytopenia and leakage of plasma, or dengue shock syndrome.

There is no reliably effective antiviral against this agent yet available. In the absence of a vaccine and antiviral drugs, the sole control measure is limiting the mosquito vectors.

The main mosquitoes, *Aedes aegypti* and *Aedes albopictus*, are potential vectors of numerous arthropod-borne viruses (arboviruses), and have now expanded from the tropics and subtropics, although *A. albopictus* still plays a relatively minor role compared to *A. aegypti* in DENV transmission.

Oral manifestations in dengue are rarely reported; gingival bleeding is the most common (Lambrechts *et al*, 2010; Mithra *et al*, 2013; Roopashri *et al*, 2015). Postoperative haemorrhage (Dubey *et al*, 2013), gingival and lip swelling (Pontes *et al*, 2014) or mucous membrane involvement with no further details (Desruelles *et al*, 1997) have also been noted. Neurological sequelae include hypoglossal palsy (Jaganathan and Raman, 2014) and taste

changes (Scully, 2013). Of interest in this context is that saliva has been attempted to be used as a diagnostic fluid for dengue fever (Ravi Banavar and Vidya, 2014).

Chikungunya

Chikungunya virus (CHIKV), a Togaviridae family alphavirus has emerged as a worldwide threat, causing fever and devitalising arthritis (the name reflects the condition of many of the stricken, 'bent down or become contorted', in the Tanzanian Makonda language) in a range of countries including many holiday destinations (Hasan *et al*, 2015).

Chikungunya virus is a mosquito-borne virus, like dengue transmitted by Aedes mosquitoes and has features of fever, headache, rash, nausea, vomiting, myalgia and arthralgia. The presentation differs in adults and children – the latter may present with fever, a rash on the face and arms and intra-oral lesions reported as 'Koplik spots' (Centers for Disease C & Prevention, 2014). Oral manifestations reported also include ulceration (MacDonald-Ottevanger *et al*, 2015) and candidiasis (Bandyopadhyay and Ghosh, 2010). Thus, Chikungunya mimics dengue and like dengue, there is no reliably effective antiviral against this agent yet available.

Indigenous to tropical Africa, recent large Chikungunya outbreaks have been reported in South-East Asia, the Indian Ocean Islands, the Caribbean, and the United States and Europe (Balkans, France, Greece, Ireland, Italy, Madeira, the Netherlands and Spain), mainly in travellers (Kumar *et al*, 2010). The rapid spread of *A. albopictus* into Europe and the Americas coupled with high viraemia in infected travellers returning from endemic areas increases the risk that CHIKV could establish itself in new endemic regions (Thiboutot *et al*, 2010). A mutation in CHIKV (E1-A226V) appears to improve virus survival in *A. albopictus* and increase its virulence (Burt *et al*, 2012).

Viral infections with significant orofacial manifestations

DNA viruses

The majority of virus infections of the oral mucosa are due to the herpes group, which are DNA viruses. The classical oral manifestations of these virus infections ranging from herpes simplex, herpes zoster to Kaposi`s sarcoma, to infections caused by EBV are adequately described elsewhere (Balasubramaniam *et al*, 2014). The description below refers to recent developments in this regard.

Herpes simplex virus infections. Herpes simplex virus (HSV) infections are increasingly seen in adults, are sometimes caused by HSV-2 and can be an SSI with stomatitis or pharyngitis (Looker and Garnett, 2005).

Herpes labialis recurrences are now recognised to be significantly common in immune defects and to occur where the innate antiviral immune response involving the interferon (IFN-λ) promoter is lacking due to polymorphisms within the IFN-λ gene (Griffiths *et al*, 2013). Therapy, despite many studies, still involves antivirals such as aciclovir or penciclovir, but hydrocolloid patches may have a place (Karlsmark *et al*, 2008; Stoopler and Balasubramaniam, 2013).

Herpes simplex virus has long been associated with cranial neuropathies and now has also been associated with Alzheimer disease (Lövheim *et al*, 2015).

Human papillomavirus infections. One of most common SSI in world, HPV can cause cutaneous or mucosal papillomas, common warts (verruca vulgaris), genital warts (condyloma acuminatum) and multifocal epithelial hyperplasia (Heck disease). Some HPV types (oncogenic or 'high-risk' HPV types such as HPV16) are now implicated in some mouth cancer, especially oropharyngeal cancer (OPC). OPC incidence has significantly increased, predominantly in economically developed countries (Scully *et al*, 1988; Scully, 2002; Chaturvedi *et al*, 2013; Brewer and Calo, 2015). HPV is a strong and independent prognostic factor for better survival of OPC (Ang, 2010; Lowy and Munger, 2010; O'Rorke *et al*, 2012),

Human papillomaviruses infection does not necessarily lead to OPC. A study of 1626 males in Brazil, Mexico, USA; 1 year showed that 0.4% acquired incident oral HPV, 1.7% acquired oral oncogenic HPV infection and 0.6% acquired oral HPV16 infection. New oral *oncogenic* HPV infections are rare and most are cleared spontaneously within 1 year (Kreimer *et al*, 2013).

The United States Food and Drug Administration (FDA) approved the quadrivalent HPV vaccine for girls in 2006 and for boys in 2011 aimed at genital, HPV-related lesions. Vaccination has proved to be successful at preventing HPV and associated cervical and other anogenital tumours. HPV vaccines are effective and also against the HPV strains that are most commonly found in the oropharynx (Wierzbicka *et al*, 2014) and have reduced infections (Herrero *et al*, 2013), but vaccination is yet to be universally recommended for all adolescents.

There are two vaccines; both regarded as safe and usually given as a three dose series.

- *Cervarix:* recommended for females from 10 to 25 years of age and protects against HPV16 and HPV18.
- *Gardasil:* recommended for 11- and 12 year-old girls and also females 13 to 26-year-old. Gardasil is also recommended for 9- to 26-year-old males to protect against some genital warts. This vaccine protects against HPV6, HPV11, HPV16 and HPV18.

Human parvoviruses. The only known parvovirus to infect humans is B19, which is transmitted by droplets, touch and occasionally in blood, and infects rapidly dividing tissues, most commonly the foetus, intestinal epithelium or haematopoietic system. B19 infection in pregnancy is associated with early foetal loss, although the probability of this is low (<10%). B19 also acutely depresses erythrocyte production, which is of little clinical significance, except in patients with other haematological diseases, particularly sickle cell disease, when haemolytic crises may be precipitated.

Parvovirus commonly causes 'fifth disease' (erythema infectiosum; slapped cheek syndrome), a mild illness with a lace-like rash on the face, trunk and extremities, usually in children. Papular-purpuric glove-and-sock syndrome is pruritus, oedema and symmetrical erythema, with a 'gloves-and-socks' distribution and oral blisters, erosions and ulcers; 50% of published cases are related to parvovirus B19 infection (Segura Saint-Gerons *et al*, 2007). Cranial neuropathies have also been reported (Soares-Fernandes and Maré, 2006). In many patients (≈80%) infected with B19, there is also arthropathy, particularly in adults. As the vaccination induced disappearance of rubella, parvovirus is the commonest cause of infection-related transitory arthritis, particularly if it affects the hands. There is no specific therapy available for parvovirus infections.

RNA viruses

Coronavirus infections. The new century has seen the emergence of several novel viruses that cause respiratory tract infections in humans including SARS coronavirus infection mainly in China, MERS-CoV in Saudi Arabia and in Asia, an H7N9 influenza A virus in eastern China, a swine-like influenza H3N2 variant virus in the USA and a human adenovirus 14p1 also in the USA. MERS-CoV and H7N9 viruses are still a major worldwide public health concern, but the pathogenesis and mode of transmission of MERS-CoV and H7N9 influenza A virus are poorly understood and their oral manifestations, if any, ill-defined (Gautret *et al*, 2014). There are no reliably effective antiviral agents available for these agents.

Hand, foot and mouth disease. Hand, foot and mouth disease (HFMD) is a common childhood illness characterised by fever and vesicular eruptions on hands and feet and in the mouth. Complications are rare, but pneumonia, meningitis or encephalitis may occur.

Hand, foot and mouth disease is not associated with one single agent; it is caused by members of the family Picornaviridae in the genus enterovirus; there are over 100 serotypes of enterovirus species A–D, which are the common cause of HFMD and illnesses in infants, such as meningitis and encephalitis (Li *et al*, 2015).

Outbreaks of HFMD have been mainly caused by two types of enterovirus A species, Coxsackievirus (CV) A16 (CVA16), or enterovirus 71 (EV71), and only sporadic cases involve other members of the enterovirus A species have been reported (Osterback *et al*, 2009). Most CVA16-associated infections cause only mild symptoms; however, some CVA16 infections can lead to severe complications and even death (Chen *et al*, 2014a).

A Chinese study of HFMD showed many patients were infected with CVA16, fewer with EV71, some were co-infected with CVA16 and EV71, and a few were infected with other enteroviruses. Upper respiratory tract infection was significantly higher in CVA16-associated patients, while neurological complications and hyperglycaemia were significantly higher in EV71-infected patients (Liu *et al*, 2014).

Enterovirus infections remain an important public health problem, and other enteroviruses and other agents are emerging as major causative agents of HFMD in some epidemics. Serotypes causing severe symptoms such as HFMD including CA16 and EV71 are decreasing, while the proportion of unidentified EV serotypes causing herpangina and viral encephalitis are on the rise (Zhang *et al*, 2015). There may be an upward trend in cocirculation of the two pathogens globally and a new role that recombinants play in the emergence of new enterovirus variants.

In 2008, a large, HFMD outbreak in Fuyang city of Anhui province in south-eastern China resulted in a large number of fatalities. Phylogenetic analyses of the entire VP1 capsid protein sequence showed isolates belonging to the C4a cluster of the C4 subgenotype, and additionally, genetic recombinations were found between the Fuyang HEV71 strain and CV-A16, resulting in a recombination virus.

In 2008, another nationwide outbreak of HFMD was reported in day care centres and schools in Finland (Osterback *et al*, 2009). From vesicle fluid specimens of hospitalised children, the authors identified the aetiological agent as coxsackievirus A6. Enterovirus D68 (EV-D68) appears to cause severe respiratory illness in children – affecting most severely those with asthma in the 2014 USA epidemic, and may cause paralyses, including affecting cranial nerves (Chen *et al*, 2014b; Foster *et al*, 2015; Maloney *et al*, 2015). There is no reliably effective antiviral against these agents yet available.

An assay using multilocus PCR and reverse transcription PCR coupled with electrospray ionisation mass spectrometry (RT-PCR/ESI-MS), which simultaneously detects and identifies human enterovirus A–D, adenovirus A–F, human herpesvirus 1–8, parvovirus B19 and polyomavirus, detected not only enteroviruses in HFMD, but also herpesviruses, polyomaviruses, adenoviruses and human rhinoviruses in 36% HFMD specimens (Chen *et al*, 2014a).

Human immunodeficiency virus. Human Immunodeficiency Virus and the orofacial implications of infection have been extensively scrutinised and reported (Greenspan, 1998; Nokta, 2008; Scully, 2014). HIV infection appeared in the 1920s in the Congo from simian origins but was not recognised until the 1980s. The pan epidemic continues to expand with worldwide latest figures of new reported infections (2014) at 2.3 m, a total of over 34 m, and infection in sexually active people now at 1 in 100 (http://www.who.int/hiv/data/en/). Worldwide, HIV is mainly heterosexually transmitted and, in the over 50s, there is a threefold increase. Africa has a known infected rate >20%, and in eastern Europe and central Asia, there has been a known increase of 250% in 10 years. UK has among highest rates of new HIV in Europe, outstripped by Portugal, Ukraine, Estonia and Russia. Most HIV infections are in heterosexuals, on vacation but many men having sex with men have HIV. HIV infection is undiagnosed in one in three affected. Multidrug-resistant HIV has appeared.

The two main viruses, HIV-1 (most common) and HIV-2, infect cells with CD4 surface receptors, mainly T-helper lymphocytes and brain glial cells, and replicate within and damage them, causing HIV disease which may be

symptomless but, over time, ultimately damages CD4+ cells crucial to host defences against fungi, viruses, mycobacteria and parasites, thus causing HIV disease and ultimately producing symptoms (mainly infections and tumours) and the acquired immune deficiency syndrome (AIDS) and a range of lesions.

HIV/AIDS common manifestations are infections, neoplasms, neurological and autoimmune disorders. Infections with viruses, mycobacteria, fungi and parasites, particularly *Pneumocystis carinii* (*jiroveci*) pneumonia and mucosal candidiasis, are common. Loss of weight and wasting ('slim disease') is common. AIDS is a lethal infection, defined as HIV infection plus 1 or more AIDS-defining illnesses and a CD4 T lymphocyte count $<200 \times 10^6$/l. Without antiretroviral treatment (ART), all eventually develop *AIDS* within 5–10 years.

Candidiasis is universal especially in HIV subtype B strain CRF19 infection, but other infections in HIV/AIDS depend also upon their environmental exposure; thus, TB is particularly common in people from Africa and in urban IV drug users in USA; leishmaniasis is common in persons from around the Mediterranean; mycoses such as penicillosis are seen mainly in northern Thailand.

Neoplasms may include virally related Kaposi sarcoma, lymphomas or carcinomas (Jose *et al*, 2013; Mthethwa *et al*, 2013; Meless *et al*, 2014; Nair *et al*, 2014).

Body fluids such as semen may contain HIV as may saliva, breast milk and blood. HIV transmission is sexual mainly: most new cases are via heterosexual intercourse. HIV can also be transmitted by infected blood or blood products, including plasma or tissues. HIV transmission by contaminated needles and syringes is an important route in injecting drug users. Cross-placental transfer is not uncommon. Transmission by needlestick ('sharps') injury is an occasional risk for healthcare workers. There is no reliable evidence for HIV transmission by normal social contact or by biting insects. Pre-exposure prophylaxis using safe sex practices plus tenofovir and emtricitabine is highly effective to prevent HIV infection. As for treatment, ART is typically effective although drugs are costly and often associated with resistance and/or adverse reactions. Immune reconstitution inflammatory syndrome (IRIS) may follow ART and can include exacerbation of some lesions such as tuberculosis, *Mycobacterium avium* complex infections, zoster, HPV, CMV, cryptococcosis and Kaposi sarcoma (Tsang and Samaranayake, 2010).

Every effort must be made to avoid needlestick (sharps) injuries, as these could transmit HIV, hepatitis viruses or other infections. In the event of such an injury, speed is of the essence, and where appropriate, counselling and postexposure prophylaxis (PEP). Current PEP for HIV (and other blood-borne agents such as hepatitis B and C) viruses in UK consists of (Samaranayake and Scully, 2013);

- HIV: tenovir, emtricitabine, lopinavir, ritonavir,
- HBV: hepatitis immunoglobulin plus HBV vaccine or booster,
- HCV: Interferon plus ribavirin.

Mumps. Mumps is a common childhood infection caused by the mumps virus (MuV), a member of the Paramyxoviridae family of enveloped, non-segmented, negative-sense RNA viruses. The defining feature of classical mumps is swelling of the parotid gland, but this is not present in all cases and it can also occur in various other disorders. Only mumps causes epidemic parotitis. Other causes of parotitis include infection by parainfluenza virus types 1 and 3, influenza A virus, Coxsackie A virus, echovirus, lymphocytic choriomeningitis virus, human immunodeficiency virus, human t lymphotropic virus 1 and non-infectious causes (e.g. drugs, tumours, immunologic diseases and salivary duct obstruction).

Mumps virus not only affects salivary glands but also other glands including reproductive glands and pancreas, leading to orchitis or oophoritis (Hviid *et al*, 2008; Ternavasio-de la Vega *et al*, 2010). Acute hormonal disturbances are common including decreased testosterone and inhibin B levels with low or normal levels of gonadotropins in 35% and a high incidence of sperm disturbance. Importantly, mumps is highly neurotropic, and central nervous system infection ensues in approximately half of cases and may lead to aseptic meningitis, viral encephalitis, and rarely deafness and pancreatitis (Rubin *et al*, 2015).

Mumps is vaccine preventable, and one dose of mumps vaccine is about 80% effective against the disease. Routine vaccination has proven highly effective in reducing the incidence of mumps and is presently used by most developed countries; however, there have been outbreaks of disease in vaccinated populations (Hviid *et al*, 2008).Since the introduction of the mumps vaccine, the age of appearance of mumps infection has shifted from children to adolescents and young adults, groups with a higher incidence of disease complications and sequelae.

In 2005, a large epidemic peaked in the UK, and, in 2006, the American mid-west had several outbreaks. In both countries, the largest proportion of cases was in young adults. In the UK, susceptible cohorts too old to have been vaccinated and too young to have been exposed to natural infections were the primary cause of the mumps epidemic. In the USA, effectiveness and uptake in combination appear not to have been sufficient to obtain herd immunity for mumps in populations such as college students.

Severe fever with thrombocytopenia syndrome virus (SFTSV) infection. An emerging infectious disease, SFTS, was identified to be associated with a novel SFTS RNA bunyavirus (SFTSV). Transmission of the disease among humans has been described, but clinical impact factors and transmission mechanisms still need further study (Bao *et al*, 2011; Li, 2015). Risk factors assessment of the person-to-person transmission revealed that the major exposure factor was blood contact without personal protection equipment. Information from this study provided solid references of SFTS incubation time, clinical and laboratory parameters related to SFTS severity and outcome, and biosafety issues for preventing person-to-person transmission or nosocomial infection of SFTSV.

There is no reliably effective antiviral against this agent yet available.

Conclusions

Viruses are ubiquitous, and they cause a wide range of human diseases, ranging from acute self-resolving conditions to fatal diseases. We continue to witness the emergence of new viruses and infections and there appear to be no signs of abeyance in the march of these elusive enemies. Apart from the acute infections with either mild or severe symptoms, a number of new and old virus infections could leave a legacy of secondary illnesses long after the primary infection has subsided. These secondary effects can also increase the propensity for chronic conditions or lead to the development of cancer. The discussion above on emerging viral diseases and old viral diseases appearing in new guises indicates the impact of such infections on the practice of dentistry not only from the perspective of oral manifestations and oral healthcare sciences, diagnosis and management but also from an equally important aspects related to infection control.

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Both authors have equally contributed to the review.

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