Promoting expertise knowledge sharing in paediatric virology: An update (Review)

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Abstract. Knowledge sharing in medical education is a continuous exchange of skills and expertise between scientists. Paediatric virology is a rapidly developing, new scientific field of medicine, which enhances multidisciplinary, expertise knowledge sharing between paediatric health professionals and scientists of different subspecialties. The present review discusses the recent core topics in paediatric viral infectious diseases discussed during the 11th Workshop on Paediatric Virology organised by the Institute of Paediatric Virology and presents its key messages, including: i) The history of smallpox vaccination; ii) the role of viral co-infections triggering invasive bacterial diseases; iii) the surge of invasive group A streptococcal disease during the post-coronavirus disease 2019 (COVID-19) era; iv) foetal brain imaging findings in maternal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection; v) the diabetogenic role of Coxsackie viruses in childhood; vi) adenovirus-related central nervous system manifestations in the paediatric population; vii) new challenges and opportunities of hepatis D virus infection in children; viii) the Swedish up-to-date human papillomavirus vaccination experience in childhood.

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1. Introduction

The recent coronavirus disease 2019 (COVID-19) pandemic has emphasized the value of innovative approaches in sharing

expertise and the importance of multidisciplinary medical education (1-3). Expert knowledge sharing is a continuous process of exchanging skills and information across medical specialties; it plays a fundamental role in medical education (4,5). Effective sharing of knowledge and experience can be achieved through international communication and multidisciplinary interaction. The creation of accessible resources including targeted workshops, can encourage this sharing and promote international knowledge interchange, networking and teamwork (6,7). The value of knowledge and skills interchange was highlighted at the 11th Workshop on Paediatric Virology organised on December 20, 2025 by the Institute of Paediatric Virology (IPV, http://www.paediatricvirology.org), located on the island of Euboea in Greece.

Taking advantage of the proceedings of this workshop, which brought together several experts in different fields, the present narrative review provides a comprehensive discussion of the historical perspectives, immunopathogenesis, epidemiology, clinical management and preventive strategies across a broad spectrum of viral infections. The topics discussed illustrated the value of multidisciplinary cooperation and knowledge interchange, with paediatric virology being the overriding theme. Such interactions can lead to collaborations, which are valuable in exposing the different experts to multiple specialties, leading to 'out-of-the box' conceptualization of the challenges and opportunities facing paediatric virology, in the post-COVID era. In this field of specialization, it is important to broaden the exposure and outlook.

The key messages of the topics discussed during the workshop (Table I) focused on the following: i) The history of smallpox vaccination; ii) the role of viral co-infections triggering invasive bacterial diseases; iii) the surge of invasive group A streptococcal disease during the post-COVID-19 era; iv) foetal brain imaging findings in maternal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection; v) the diabetogenic role of Coxsackie viruses in childhood; vi) adenovirus-related central nervous system (CNS) manifestations in the paediatric population; vii) new challenges and opportunities of hepatis D virus (HDV) infection in children; and viii) the Swedish up-to-date vaccination against human papillomavirus (HPV) experience in childhood.

2. On the history of smallpox vaccination: Dr Emmanuel Timonis, Dr Jacob Pylarinos and the Greek women of 18th-century Constantinople

The evolution of vaccination can be traced back to the early 18th century, when variolation, which involved the deliberate insertion of smallpox matter into the skin of healthy people, led to a mild infection and subsequent immunity (8). Historical consensus credits the influential role of Lady Mary Wortley Montagu, wife of the British ambassador to the Sublime Porte, in promoting smallpox inoculation among the English elite (9). However, more recent research reveals the key contribution of two Greek medical professionals, Dr Emmanuel Timonis from Chios (1669-1720) and Dr Jacob Pylarinos from Cephalonia (1659-1718) (10-16). Their reports to the Royal Society in London introduced variolation to Western medicine and transformed folk wisdom into documented, evidence-based medicine, laying the critical groundwork for Dr Edward Jenner's development of the safe cowpox vaccine almost a century later.

The biographies of these two Greek physicians and diplomats merit closer examination in order to acknowledge the role of lesser-known individuals, whose status did not gain historical visibility, in the practice of vaccination. Both Timonis and Pylarinos had witnessed the effective application of variolation across multiple regions of the eastern Mediterranean and, by documenting the method in their writings, they significantly contributed to the legitimisation of folk medical practices commonly employed within the Greek communities of the Ottoman empire.

Variolation was extensively practiced throughout the Ottoman empire, with women serving as key agents in its dissemination (10,17,18). Describing how experienced older women 'engrafted' children with smallpox matter in communal gatherings in Constantinople 'every autumn in the month of September', Lady Montagu wrote that 'the Grecians have commonly the superstition of opening one [wound] in the middle of the forehead, in each arm, and on the breast to mark the sign of the cross' (19). In his account, Pylarinos also noted that women made incisions in the form of a cross as a ritual accompaniment that would ensure success.

Although variolation was commonly perceived as both a religious act and an effective prophylactic measure, it found strong resistance by the Christian churches in Constantinople that viewed it as a usurpation of the divine prerogative. The French traveller Aubry de la Motraye relates how, in the face of fierce ecclesiastical opposition, Dr Timonis and his friend Dr Charles Le Duc, another doctor resident in the Ottoman capital, defended variolation as a life-saving prevention method: 'I remember the doctors Timonis and Le Duc, both great promoters of inoculation at Constantinople, having drawn the Greek and Armenian clergy upon their backs, as well as the Romish, on that account, answered them by way of raillery that their invectives against the inoculation, as disturbing the order of Providence, hinted that death was more agreeable to that order than life, but seemed to proceed only from a selfish spleen, because they were, by this method of practice, deprived of the profit of burying so many children as died before every day of the smallpox' (20).

Dr Timonis and Dr Pylarinos are now recognised as key precursors to Dr Edward Jenner, whose development of smallpox vaccination using cowpox in 1796 would eventually supplant variolation (Fig. 1). Taken together, the illustrious careers of these two Greek physicians challenge Eurocentric assumptions that locate the origins of modern medicine solely in Western Europe. But they also destabilise mainstream histories of vaccination that present medical innovation as the exclusive domain of elite, male physicians. Instead, they reveal a far more complex history of healthcare-one shaped by gendered labour, vernacular knowledge and transcultural exchange. While Dr Timonis and Dr Pylarinos provided the scientific framing that appealed to European audiences, their medical reports incorporated indigenous understandings of disease and prevention that had been current in the multi-ethnic and multi-religious milieu of the Ottoman empire for centuries. In this regard, their life stories place smallpox inoculation at the crossroads of medical history, social studies of science,

Table I. Key messages from the 11th Workshop on Paediatric Virology organised by the Institute of Paediatric Virology.

Topic	Key messages
Smallpox vaccination (8-20)	Dr Emmanuel Timonis (1669-1720) from the island of Chios and Dr Jacob Pylarinos (1659-1718) originating from the island of Cephalonia played a crucial role in validating folk medical practices against smallpox, which were prevalent among the Greek Orthodox communities, and introducing them into Western medicine, during the early eighteenth-century. Throughout the history of the Venetian and Ottoman empires, the folk medical practice of smallpox inoculation highlights the contribution of Greek women in early eighteenth-century Constantinople, which should be integrated into the mainstream history of vaccination.
Viral and bacterial co-infections (21-41)	Viruses can predispose to bacterial invasion through epithelial disruption, altered cytokine responses, and transient immune suppression even in previously healthy hosts. Recent paediatric cohort studies demonstrate higher incidence of pneumonia as well as higher PICU admission rates in children with viral co-infection, underscoring its role in severe disease. The COVID-19 pandemic and implementation of NPIs profoundly disrupted the epidemiology of communicable diseases. The subsequent 'immunity gap', driven by reduced exposure to pathogens and decreased vaccine uptake, contributed to atypical surges in respiratory infections once NPIs were lifted. This phenomenon coincided with a remarkable rise in iGAS disease in children. The pre-pandemic rise in iGAS disease followed a sharp decline during the 2020-2021 lockdown era along with the suppression of viral circulation. From late 2022, however, both North America and Europe reported early and severe rebounds of paediatric iGAS disease, temporally aligned with large outbreaks of influenza and RSV. These findings highlight the importance of strengthening integrated surveillance of respiratory viruses and iGAS, alongside reinforcing vaccination programmes against influenza viruses, RSV and VZV, as key strategies to mitigate future invasive bacterial outbreaks in the post-pandemic era.
SARS-CoV-2 (42-53)	In mild, vaccinated/Omicron-era's, maternal SARS-CoV-2 infection, there are usually no detectable findings on foetal brain MRI regarding foetal brain growth and cortical evolution compared with controls. In the presence of foetal brain abnormalities, usually following severe maternal infection, the most likely mechanism is placental vascular/inflammatory injury rather than direct foetal brain infection. Foetal brain MRI is indicated in higher-risk scenarios, where placental assessment and postnatal follow-up imaging should be considered.
Adenovirus (54-70)	HAdV infection is rarely implicated in CNS disorders, but it can present with signs and symptoms ranging from mild altered consciousness and seizures to encephalitis and severe encephalopathy. Often the diagnosis is not based on HAdV detection in the CSF or pleocytosis, but rather on a positive PCR test from another site, mainly nasopharynx or stool. Management of CNS manifestations requires hospitalisation and supportive care; outcome is usually favorable with most patients returning to normal life or experiencing only minor sequelae.
Coxsackie virus (71-83)	The destruction of the pancreatic insulin producing cells is a result of genetic susceptibility and environmental interaction, with gradual progression over many months or years. Among several viruses reported as diabetogenic, the most studied are CVB and particularly, the B4 subtype. There is some evidence that antiviral therapies against CVB can reverse the diabetogenic process, and thus a safe and effective vaccine could potentially preserve insulin production by preventing the disease itself.
HDV (84-109)	A number of studies have shown relatively high prevalence of anti-HDV seropositivity in HBV HBsAg-positive pregnant women. Preterm delivery and poor outcomes can occur in HBV/HDV infected pregnant women. Assessment of the seroprevalence of HDV in pregnant women and perinatal MTCT is under-represented globally, and should be prioritised in order to prevent PMTC HDV (and HBV).

Table I. Continued.

Topic	Key messages
	The birth dose vaccination against HBV, followed by completion of a subsequent 3-dose series in infants at 6, 10 and 14 weeks, can protect against both viral infections as well as liver cancer. Although HBV vaccination has resulted in the decrease of HDV incidence in areas where vaccination has been successfully implemented, high risk practices, such as tattooing and scarification, multiple pregnancies and immigration from endemic HDV regions have been identified as risk factors leading to an increase in prevalence of HDV in areas of low endemicity. Historically, the standard of care for the prevention of HDV-associated liver disease progression has been the use of peg-interferon-α. In recent years, several new therapies have emerged, including bulevirtide, the first agent approved for use in chronic HDV infections by the EMA.
HPV vaccination (110-126)	In Sweden, HPV vaccination was available early on after 2006 when the first HPV vaccine was acknowledged by the FDA; current guidelines generally recommend two doses for children below 15 years of age, while for individuals above 15 years of age, three doses are recommended. In 2010, it was possible for 10-12-year-old girls to be HPV vaccinated free of charge, but it was not until 2012, that HPV vaccination was offered to girls of the same age group through the school based-vaccination programme. In 2020, also boys, 10-12 years of age, were offered HPV vaccination through the school-based vaccination programme. Research has shown that HPV prevalence of the vaccine types has decreased considerably in both the genital and oral tracts, particularly among vaccinated youth, while herd immunity has also been observed.

PICU, paediatric intensive care unit; COVID-19, coronavirus disease-2019; NPIs, non-pharmaceutical interventions; iGAS, invasive group A *Streptococcus*; RSV, respiratory syncytial virus; VZV, varicella zoster virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; MRI, magnetic resonance imaging; HAdV, human adenovirus; CNS, central nervous system; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; CVB, Coxsackie group B; HDV, hepatitis D virus; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; MTCT, mother to child transmission; EMA, European Medicines Agency; HPV, human papillomavirus; FDA, Food and Drug Administration.

and cross-cultural perspectives on health and healing, while also shedding light on people, places, and stories that were once central but have since faded into obscurity.

3. Viral co-infections: Immunological and pathogenic mechanisms triggering invasive bacterial disease

Viral infections can predispose to invasive bacterial disease. Looking back in history, during the 1918 Spanish flu pandemic, as well as the 2009 H1N1 influenza season, streptococcal superinfections with *Streptococcus pneumoniae* and group A *Streptococcus* (GAS), as well as *Staphylococcus aureus* were associated with increased mortality rates (21-23). Basic research has shown that this bacterial invasion may take place through direct epithelial disruption in the respiratory tract as has been observed with influenza viruses that facilitate streptococcal adherence. Similarly, varicella zoster virus (VZV) may breach the skin, leading to invasion by bacteria, paving the way to GAS necrotizing fasciitis (24). Viral co-infections can trigger immune modulation and dysregulation. Influenza type A infection induces type I and type II interferons and cytokines (e.g. tumour necrosis factor α (TNF-α), interleukin (IL)-12, interferon (IFN)-γ that deplete or suppress alveolar macrophages and neutrophil function by inhibiting the production of some key antibacterial proinflammatory cytokines, such as IL-23 and IL-17. Another suppressive mechanism is the impaired function of immune cells, such as dendritic cells, as well as the proliferation and cytotoxicity of T-cells and natural killer cells (25). In murine models, a prior influenza infection caused elevated systemic cytokines (IFN-γ, TNF-α, etc.), which paradoxically hampered GAS clearance from the bloodstream and increased mortality (22).

Although less extensively studied, respiratory syncytial virus (RSV) likely functions in a similar manner. RSV causes airway epithelial damage and strong inflammatory responses, which, in animal models, enhance susceptibility to bacterial superinfection (e.g., with *Streptococcus pneumoniae*) (26). Epidemiologically, RSV peaks coincided with invasive GAS (iGAS) outbreaks, and co-detection of RSV with iGAS is often reported (24). Similar to influenza viruses, RSV can skew cytokine profiles, including IL-6 and IFNs, and impair neutrophil trafficking, potentially promoting streptococcal invasion. Notably, an Australian paediatric surge study found that children with viral co-infection (often with influenza viruses or RSV) were almost twice as likely to develop severe iGAS as those without viral co-infection; these mechanisms likely explain the post-COVID-19 pandemic iGAS resurgences coincide with unprecedented respiratory virus waves (27).

Chicken pox caused by VZV is a well-known potent risk factor for iGAS in children (28). Apart from skin lesions providing portals, VZV infection causes transient immune suppression (e.g., of neutrophils and cell-mediated

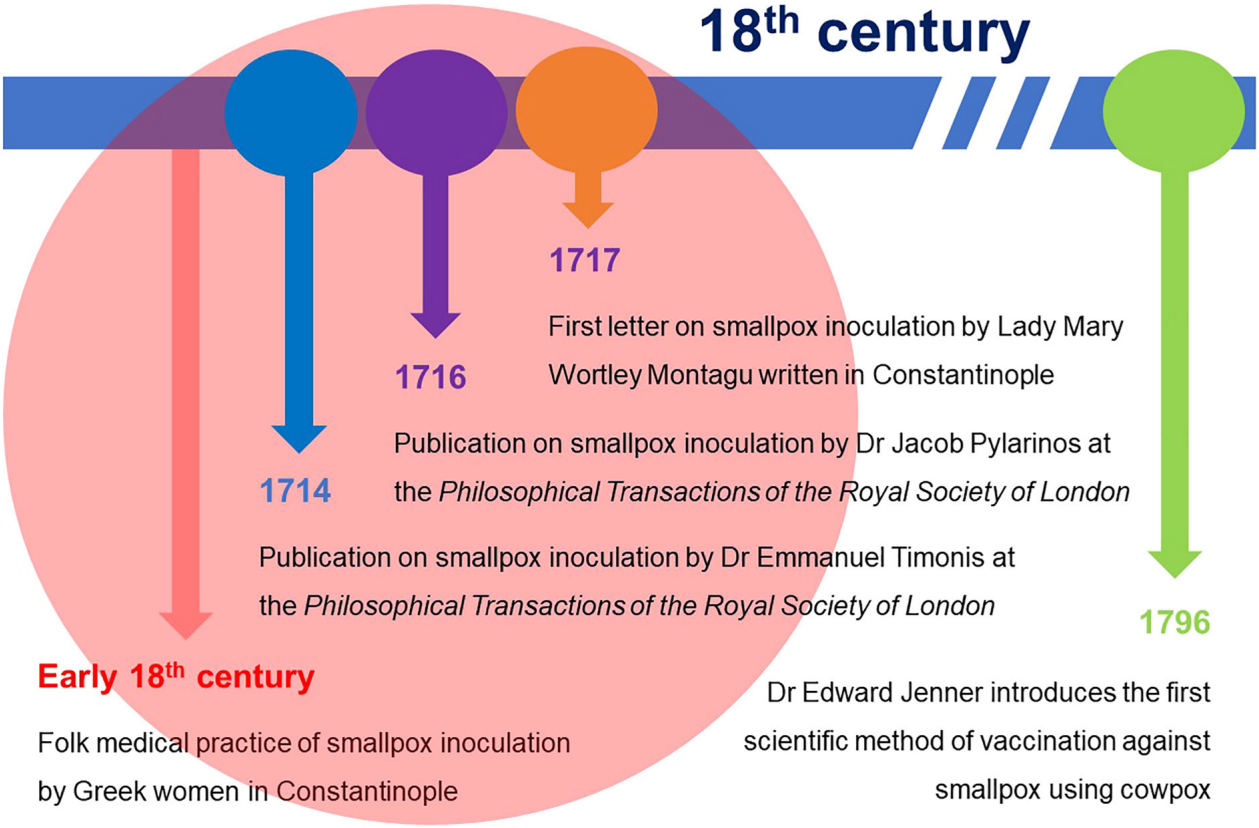

Figure 1. Dr Edward Jenner's precursors against smallpox during the 18th century A.D.

immunity) (29). Prior to the introduction of vaccination, data show that 15-36% of paediatric necrotizing fasciitis cases were associated with VZV infection. Of note, iGAS superinfections sometimes occurred even without obvious skin lesions, implying a systemic innate immunosuppression due to the VZV itself (21,29). Consequently, strengthening the surveillance of viral and bacterial disease burden, particularly during extreme situations, such as pandemics caused by novel strains or the implementation of strict public health measures, may facilitate the early recognition and management of future outbreaks (Fig. 2).

4. The role of viral co-infection in the surge of invasive group A streptococcal disease during the post-coronavirus disease 2019 (COVID-19) era

The COVID-19 pandemic along with the implementation of non-pharmaceutical interventions (NPIs) significantly disrupted the epidemiology of many communicable diseases. The 'immunity gap' theory has been conceived and adopted by experts in the field as a plausible reason for the upsurge of respiratory illnesses when NPIs were lifted across the globe (30,31). Apparently, reduced exposure to respiratory pathogens, as well as a significant decrease in the uptake of routine vaccinations observed during the pandemic, led to an attenuated depletion of immune stimulation and a 'herd immunity' gap, in the population level. Moreover, viral and bacterial respiratory pathogens have explosively resurged in various time frames to fill the gap of prolonged circulation disruption (32,33).

This is partly depicted in the post-pandemic epidemiological trends in Europe and the USA that exhibited global outbreaks of viral infections and were associated, at least temporally, with GAS surges and iGAS cases, in particular. Prior to the COVID-19 pandemic, the incidence of iGAS had been rising in a number of countries, including the USA and the European Union (34); however, from 2020 to 2021, iGAS rates plummeted worldwide as NPIs halted both GAS and viral transmission. Globally, respiratory viruses, such as influenza viruses and RSV, also nearly vanished in that period, leaving a population with reduced recent exposure to these common pathogens (31,34).

After NPIs were lifted in 2022, the US Centers for Disease Control and Prevention (CDC) recorded a 'high season' rebound with a paediatric iGAS rise earlier than usual (September-November), which also coincided with surges of influenza viruses and RSV (33). Similarly, several European countries, including the UK, Ireland, The Netherlands, Sweden and France, exhibited an unusual rise in paediatric iGAS cases from autumn 2022 onward that coincided with epidemic peaks of viral respiratory illnesses (35-38). In addition, a population-based case series covering a 30-year period (1992-2023) of paediatric iGAS infections in Canada highlighted the increased number of viral co-infections, as well as a significant rise in iGAS infections of the upper and lower respiratory tract in the post-pandemic period, statistically associated with increased paediatric intensive care unit (PICU) admissions. Notably, PICU admissions due to iGAS rose from 9.2% during the 1992-2001 period to 26.8% during the 2022-2023 period (39).

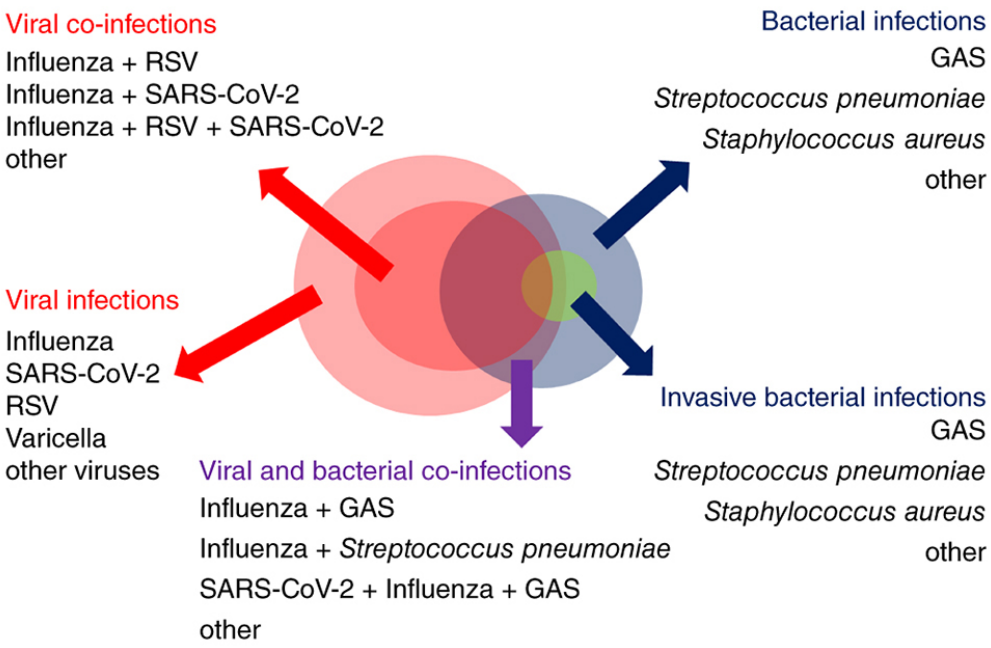

Figure 2. Evaluating the co-existence of viral infections, viral co-infections, bacterial infections and invasive bacterial infections. RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; GAS, group A *Streptococcus*.

Despite the large increase in lower respiratory tract infections (LRTIs), as well as iGAS disease in children, in the aftermath of the COVID-19 pandemic, studies have shown that there was some benefit from the mitigation strategies in terms of averted hospitalisations and iGAS disease morbidity and mortality (40,41). A lesson well-learned from the COVID-19 pandemic is that enhanced public health measures such as sophisticated surveillance systems both for iGAS and respiratory viruses will shed light on the dynamics of pathogen-pathogen interactions. Similarly, solid and uninterrupted immunisation programmes against common viruses such influenza viruses, VZV and RSV may avert future outbreaks of invasive bacterial disease and lead to a less vulnerable paediatric population.

5. Foetal brain MRI findings in maternal SARS-CoV-2 infection

Maternal SARS-CoV-2 infection during pregnancy has raised concerns about the *in utero* development of the foetal brain, due to the known effect of other maternal infections on the anticipated course of normal neuronal migration (42), but also due to the documented hypercoagulable predisposition of certain subjects affected by SARS-CoV-2 (43). During the recent years, SARS-CoV-2 infections have revealed numerous neurological side-effects in children and adults, of which imaging findings may be subtle or absent (44). Limited information was available during the early years about the effects on foetal brain development and imaging findings in the case of maternal SARS-CoV-2 infections during pregnancy.

Foetal brain magnetic resonance imaging (MRI) is a well-established method that provides a detailed evaluation of the foetal brain, especially of the cortical development, and complements high-quality ultrasound, in order to clarify ambiguous or subtle sonographic findings (45). Current evidence suggests that uncomplicated maternal infection, particularly in vaccinated, Omicron-era cohorts, is not consistently associated with abnormal foetal brain growth or cortical maturation on foetal brain; specific patterns have, however, been described in selected subgroups, via indirect placental pathways (46,47). In cases with placental and neonatal MRI findings, the most likely pathogenic mechanisms are assumed to involve vascular and inflammatory procedures rather than direct foetal neurotropism (48-51).

Placental vascular lesions and placentomegaly were detected on antenatal MRI in prospective studies during the variant waves, whereas foetal effects depended on certain variants and maternal illness severity (46). Of note, a case-control foetal brain MRI study, assessing brain biometry and cortical development, resulted in no significant differences in the pattern of sulcation or cortical mantle thickness among foetuses of mildly symptomatic mothers vs. controls, concluding that cortical maturation is not affected in low-severity maternal infection (47). Although slightly discordant, these results suggest that even in presence of placental pathology, if maternal disease is mild and oxygenation is preserved, foetal brain morphology is preserved.

A longitudinal cohort, using quantitative neonatal brain MRI, found subtle differences in early newborn brain development following antenatal exposure, implicating white-matter and microstructural pathways, lacking universal significant functional effects (48). Parallel multimodal foetal MRI work during the pandemic examined association of maternal psychological distress with altered foetal brain measures; the concept that maternal immune/psychosocial activation can shape foetal brain microstructure is supported, even in the absence of severe maternal respiratory disease (49,50). A mechanistic review synthesising placental angiotensin-converting enzyme 2 expression, maternal cytokine signalling (e.g., IL-6/IL-17) and vascular injury describes how placental insufficiency and inflammation

could yield hypoxic-ischemic susceptibility of the developing brain, aligning with perinatal imaging phenotypes (51).

Severe post-COVID-19 placentitis, as described by pathology series, appears to represent a vascular route of injury as it is characterised by massive perivillous fibrin deposition and trophoblast necrosis, which results in foetal hypoxic-ischemic demise without necessarily concurrent foetal infection (50). This mechanism provides a plausible substrate for the rare foetal and neonatal MRI lesions reported following severe maternal COVID-19. These usually include thalamic infarction and white-matter injury (46). On the contrary, large prenatal imaging cohorts from the Omicron/vaccinated period show preserved overall foetal brain growth on foetal brain MRI, suggesting variant tropism and immunity meaningfully modulate risk (46,52).

Indications to consider foetal brain MRI in maternal COVID-19 include the following: i) Severe/critical maternal disease; ii) severe sonographic abnormalities (growth restriction, doppler changes); iii) suspected placental disease; and iv) severe maternal distress with concerns about foetal neurobehavior. In these cases, foetal brain MRI protocols should emphasise in volumetry, cortical evaluation, diffusion sequence (ADC/DTI) for assessing white matter and placental protocol when feasible. Additionally, counselling should balance reassuring data for mild maternal disease with vigilance for placental-mediated injury in severe cases (46-53). Ongoing longitudinal studies are required to connect prenatal MRI with later neurodevelopment and delayed brain imaging of the child.

6. Adenovirus-related CNS manifestations in children

Human adenoviruses (HAdVs) are medium-sized, non-enveloped viruses with an icosahedral nucleocapsid enclosing a double-stranded DNA genome of ~34 kb in length. They consist of a family of >60 serotypes divided into seven subgroups (A through G) based on immunological, biological and biochemical characteristics (54). HAdVs are among the most common viruses isolated from young children with febrile illnesses. Pharyngitis, otitis media, bronchiolitis and pneumonia are the main presentations of respiratory tract infections (54-56). Pharyngoconjunctival fever and diarrheal illness are also frequent adenoviral syndromes. Although serotype 41 was detected in 65% of the tested cases in the UK, its role as the causative agent of the 2022 outbreak of severe acute hepatitis in children remains uncertain (57).

HAdVs have been rarely described as causes of CNS disease, particularly in immunocompetent children and most publications consist of case reports or small case series. The clinical spectrum is highly variable, ranging from mild altered consciousness to severe encephalopathy and acute necrotising encephalitis (55,58,59), with seizures and encephalitis-meningoencephalitis being the most common presentations. Serotype C was documented as the cause of meningoencephalitis and severe sepsis in a previously healthy 15-month-old girl (60) and type 7 in a fatal case of a 20-month-old boy (61). Straussberg *et al* (62) described 7 infants 7-34 months old with transient encephalopathy, characterised by decreased level of consciousness without seizures or signs of meningeal involvement associated with adenoviral infection. Concomitant respiratory and gastrointestinal symptoms were frequently observed. In the systematic review by Schwartz *et al* (63), 5% of children with confirmed HAdV infection exhibited neurologic symptoms with an encephalitis incidence of 0.4%, while 3.3% presented with seizures; alternatively, 1.9% of encephalitis cases were attributed to HAdV. A similar rate (3.3%, 109 out of 3298) of children with culture-confirmed HAdV infection and neurological dysfunction was recorded in a retrospective study from Taiwan (64). Both studies demonstrated a predominance in males, mostly in children <5 years of age. In the majority of the studies, the incidence of HAdV-confirmed encephalitis was estimated between 1.08 and 1.5% (65-67). However, in a cohort study conducted in Finland, HAdV was implicated in 5% of childhood encephalitis cases (68), highlighting the importance of clinical suspicion and advanced diagnostic tools, given that a significant proportion of viral encephalitis cases remain unattributable.

Certain HAdVs serotypes are associated with distinct clinical manifestations and serotypes 1, 2, 3, 4, 5, 6, 7, 11, 12, 26, 32 and 41 have been implicated in CNS disorders; however, the pathogenesis remains unclear. HAdVs rarely invade the CNS, since their receptors are expressed at low levels in brain tissue. It has been proposed that the adenovirus penton antigen, a component of the capsid, induces a T-lymphocyte-mediated response that triggers a cascade leading to perivascular oedema, vascular wall degeneration and presence of inflammatory cells within the brain. This hypothesis may explain the severity of CNS disorders in individuals with immunodeficiencies.

In a number of studies, the diagnosis of HAdV-associated CNS infection was not based on the detection of HAdV in cerebrospinal fluid (CSF) by viral culture or PCR, but rather on a positive PCR test from another site (nasopharynx, throat, sputum or stool) in children with neurologic manifestations (58,59,62,64). Indeed, in the review by Schwartz *et al* (63), HAdV was identified in CSF in only 15% of cases. In recent years, this rate has increased due to the widespread use of multiplex real time PCR assays (65). CSF findings are often unexceptional, with numerous patients demonstrating normal profiles (59,62) or only mild pleocytosis (white blood cells, <30/mm^3) (63-65). There are limited data regarding neuroimaging or electroencephalogram (EEG) findings. Several patients exhibit abnormal results on an EEG examination, most commonly generalised slow rhythm and epileptiform discharges (62,64,67); more rarely, abnormal findings are revealed on brain MRI (58,64,67).

The majority of HAdV infections are self-limiting and treatment is mainly supportive. Patients with CNS involvement require hospitalisation, even admission to the PICU, if intubation is necessary for airway protection or status epilepticus (60,61). Antiviral therapy with cidofovir, ganciclovir, ribavirin and vidarabine has been used in case reports or uncontrolled series (69). Among these agents, cidofovir appears to be most the effective; however, its use is recommended for disseminated disease and immunosuppressive patients due to severe nephrotoxicity (69). T-cell immunity is crucial for the recovery of adenoviral infections (70). Hematopoietic stem cell or solid organ transplant recipients may benefit from transfer of donor-derived, virus-specific memory T-cells. In the study by Leen *et al* (70), the management of HAdV infections in 17 paediatric stem cell transplant recipients with banked third-party virus-specific T-cells from individuals with

common human leukocyte antigen polymorphisms, resulted in a complete or partial response in 78% of patients.

Although deaths have been reported (61,63), the majority of children suffering from HAdV-associated neurological disorders experience a favourable outcome (59,60,62,65). In a Taiwanese study >90% of children with CNS involvement returned to normal health, 6.5% recovered with minor sequelae (seizure disorder) and no deaths were recorded (64). According to Tian *et al* (66), 42% of affected individuals developed complications, but only 1% were associated with CNS such as epilepsy, cerebral hernia and paralysis. A young age, particularly <2 years, convulsions and pre-existing conditions are predictors of a worse prognosis (64). When analysing the causes of death, all fatalities are attributed to respiratory insufficiency, septic shock and multiple organ dysfunction rather than neurologic manifestations. This highlights the importance of monitoring systemic complications in addition to neurological symptoms.

7. Diabetogenic role of Coxsackie viruses: The feasibility of a vaccine

Type 1 diabetes (T1D), also known as insulin-dependent diabetes mellitus, is an autoimmune disease characterised by inadequate insulin production from the pancreatic β-cells in the pancreatic islets of Langerhans (71). The destruction of the pancreatic insulin producing cells is a result of genetic susceptibility and environmental interaction, with gradual progression over many months or years (71-73). Viral infections have been extensively studied and associated as the most common trigger factors of autoimmune conditions in general and T1D in particular (74). Studies are trying to clarify whether such infections can be the cause of pancreatic autoimmunity or, once the autoantibodies against islet autoantigens are present, then the viral infection accelerates the disease process and establishes the clinical outcome (73,74). It was in 1899, when Dr Henry Fauntleroy Harris first suggested that T1D developed due to a viral infection (measles) (75). Among several viruses reported as diabetogenic, the most extensively studied are Coxsackie viruses group B (CVB), particularly B4 subtype (76,77). The theory that links the enteroviral infection with T1D, is believed to have existed for >40 years (71).

There are scientific observations connecting exposure to enteroviruses, *in utero* and in childhood, to the damage of β-pancreatic cells and the establishment of diabetes, caused by a possible migration of the virus from the mucus membrane of the intestines to the pancreas (71,78,79). Such a hypothesis may be supported by the observation that there is a rise in the prevalence of T1D following enterovirus epidemics (80). In the DiViD study (Diabetes Virus Detection Study), small pancreatic tail tissue particles from living adult patients newly diagnosed with T1D (4-9 weeks after diagnosis) and from controls, were analysed to detect possible mechanisms that interfere with the destruction of the β-cells (e.g., cell stress, DNA damage, inflammation etc.) (72). Tissues from nose, throat, intestine, blood and stools were also taken and stored, for virus examination and future investigation. A low-grade enteroviral infection was detected in the pancreatic tissue of all adult patients (72). In a phase 2, randomised, placebo-controlled, double-blind trial (DiViD Intervention Trial) which included 96 children and adolescents (6-15 years of age) with newly diagnosed T1D, when antiviral treatment was given, it led to the preservation of the residual insulin production compared with placebo (72,81).

Several autoantigens within the pancreatic β-cells may play a key role in the onset or progression of autoimmune islet injury, such as glutamic acid decarboxylase (GAD), insulin, insulinoma-associated protein 2 (IA-2) and zinc transporter (ZnT8) (82). GAD can be found in the islets, but also in the central nervous system and testes (82). Antibodies against GAD are detected in almost 70% of patients with T1D at the time of diagnosis. Molecular mimicry due to homology between GAD and F2C protein of CVB subtype B4 may be a possible mechanism for T1D development (78,79). Studies have revealed the presence of CVB-specific immunoglobulin M (IgM) in 39% of children with new-onset T1D against 6% of normal children; the existence of significantly higher Coxsackie virus antibody titres in pregnant women whose children developed T1D in comparison with other pregnant women whose children did not become diabetic and siblings of diabetic children who developed T1D themselves, had experienced enteroviral infection 2-fold higher than siblings who remained non-diabetic (74,78,79,82).

As aforementioned, the tropism of CVB for pancreatic tissue appears very strong, suggesting that scientific research should be directed toward developing appropriate therapies, but most importantly in producing a vaccine against the viruses, to prevent acute infection and potentially many cases of T1D (74). Several antiviral agents are being tested to halt the viral invasion. During the DiViD Intervention study, the combination of pleconaril and ribavirin was administered to children and adolescents with newly diagnosed T1D stage 3 for 6 months, leading to the preservation of the residual insulin production after 1 year, compared with placebo (72,81). Natural remedies such as flavonoids targeting 2C CVB protein appeared promising as antiviral therapy in the study by Ullah *et al* (71); however, it remains unclear whether the effect of the drug reduced the diabetogenic process.

The observation that the offspring of mothers with anti-CVB antibodies exhibit a ~50% reduction in the CVB-infection-associated risk of islet autoantibodies, stands as a strong advocate for the preventive role of a vaccine against the disease and the risk of T1D (74). A formalin-inactivated non-adjuvanted pentavalent intramuscular vaccine comprising the five most common serotypes (CVB1 to CVB5) is being tested (phase I safety trial) in healthy adults (83); studies with similar vaccines in mice and non-human primates, have demonstrated that these have proven to be safe, immunogenic and preventive of CVB infection, as well as of CVB-induced diabetes and CVB-myocarditis (83). In the event that such a vaccine turns out to be preventive, it will be feasible to demonstrate whether the hypothesised diabetogenic action of CVB types is really causal (74,83).

8. Hepatitis D virus infection in children: Challenges and opportunities

HDV, a member of the genus *Deltavirus*, is an RNA satellite virus, that can replicate only in the presence of hepatitis B virus

(HBV), as it requires the envelope protein of HBV to exit the liver cell. An individual can be infected concurrently with both viruses or chronic HBV carriers can be super-infected with HDV, resulting in the most severe form of viral hepatitis. Children with HDV infection exhibit more aggressive liver disease with an early progression to cirrhosis, mainly in males of a younger age (84-86). Within 2.3 years of prospective follow-up, a higher incidence was recorded in children in Greece compared with adults (2.2 new HDV-infected adults vs. 8.7 children per 1,000 HBsAg-positive annually) (86). Recently, HDV has been classified as a carcinogenic virus (87). The birth dose vaccination against HBV, followed by completion of a subsequent 3-dose series in infants at 6, 10 and 14 weeks (88), can protect against both viral infections and liver cancer.

The standard serological marker for both clinical diagnosis and epidemiological surveillance is antibody against HDV (anti-HD), whereas the detection of HDV-RNA in serum is the biomarker for active infection (89). The lack of surveillance, standardisation of assays, diagnosis and data render the global prevalence of HDV difficult to map. A previous meta-analysis estimated a global HDV prevalence of 4.5% among all HBV carriers (90). However, areas of high endemicity include Africa and Asia, with Mongolia documenting the highest documented prevalence of 60% of HBV carriers being infected with HDV (91). Following a systematic review of HDV seroprevalence in HBsAg-positive individuals in sub-Saharan African, marked differences were observed in the different geographical regions: western Africa had a pooled seroprevalence of 7.33 and 9.57% and Central Africa with 25.6 and 37.8%, in the general population and liver disease patients, respectively, whereas eastern and southern Africa had lower levels of 0.05% in the general population (92). Among HBsAg-positive individuals 7.5% tested anti-HDV positive in the Ukraine in 2021 (93), whereas a study conducted in Oman revealed a 5.63% prevalence rate (94). In Bulgaria, the prevalence was found to be 16.6% in liver disease patients, which is comparable with the prevalence found in this population in Spain, but lower in than that observed in Greece (95). However, comparisons are confounded by different methods of surveillance and diverse populations surveyed.

Although HBV vaccination has resulted in the decrease of HDV incidence in areas where vaccination has been successfully implemented (96), high-risk practices (tattooing and scarification), multiple pregnancies and immigration from endemic HDV regions have been identified as risk factors leading to an in increase in prevalence of HDV in areas of low-endemicity (95). Changes in the epidemiology of HDV have been described in European countries with high levels of immigration including Italy, Greece, Spain and the UK (97-99).

As HDV is a blood-borne virus similar to HBV and HIV, it may be transmitted from mother-to-child. Several studies have demonstrated a relatively high prevalence of anti-HDV seropositivity in HBsAg-positive pregnant women: 4 to 32.3% in Cameroon, 14,7% in Mauritania, 20,3% in Pakistan and 3% in France (100-104). Preterm delivery and poor outcomes can occur in HBV/HDV-infected pregnant women (105). The assessment of the seroprevalence of HDV in pregnant women and perinatal mother-to-child transmission (MTCT) is under-represented globally (106) and should be prioritised in order to prevent MTCT of HDV (and HBV), and the consequent chronicity of viral infections and the development of hepatocellular carcinoma.

Historically, the standard of care for the prevention of HDV-associated liver disease progression has been the use of peg-interferon-α (107). In recent years, several novel therapies have emerged, with bulevirtide, an entry inhibitor, the first agent approved for use in chronic HDV infections by the European Medicines Agency (EMA) (108). Bulevirtide is administered daily by subcutaneous injection and is not curative, requiring lifelong therapy. The currently available tools for both the prevention and the treatment of HDV should prevent the positive testing of children to HDV. The increased awareness of this life-threatening infection, concerted surveillance and the implementation of preventive measures are therefore essential to ensure the elimination of HDV as a public health concern (109).

9. School-based HPV vaccination in childhood: The Swedish experience

HPV is a family of >200 members of small double-stranded DNA viruses with circular genomes of ~7,900 bp (110). The genome is arbitrarily divided into an early region, a late region and the long control region. The early region codes for the functional proteins E1, E2, E5-E7, where E6 and E7 are in high-risk HPV types regarded as oncogenes, while the late region codes for the major and minor capsid proteins L1 and L2 respectively (110). Notably, in this context, it was known early on that the L1 protein can self-assemble into virus-like particles and these are then used as antigens in the HPV vaccines available today (111,112). Although ample knowledge was available about the association of HPV with cervical cancer in the 1980s, it was not until 1995 that HPV16 and 18, and potentially some other HPV types were acknowledged as being carcinogenic for humans by the International Agency on Research against Cancer (IARC) (113).

Studying HPV in head and neck cancer, the research team at the Department of Oncology-Pathology at the Karolinska Institute (Stockholm, Sweden) detected HPV in tonsillar squamous cell carcinoma and base of tongue squamous cell carcinoma (114,115). Shortly thereafter, the same research team found that the prevalence of HPV was increasing in these tumours and that they were increasing epidemically in incidence, and this was quite unexpected (116-118). However, similar data were also obtained from the USA and other Western countries (119,120). During the same time period, in 2006, the first HPV vaccine was approved by the Food and Drug Administration (FDA) (112). This led the research team at the Department of Oncology-Pathology at the Karolinska Institute to initiate a contact with the Swedish Institute for Disease Control, and in parallel, to investigate the presence of HPV in the genital and oral tracts of youths aged 14-23 years at a youth clinic in Stockholm. Notably, between 2008-2010, the prevalence of genital HPV (69.5%) was high in non-vaccinated women at a youth clinic in Stockholm (121). Moreover, during the same period at the same youth clinic, oral HPV infection was also common in both young women and men (122). These data initiated a study on oral HPV infection in school classes, and the team's work to promote HPV vaccination within the school-based-vaccination programme (123).

In Sweden, although already since 2010, it has been possible for 10-12-year-old girls to be vaccinated for HPV free of charge, it was not until 2012 that the HPV vaccination option was offered to them through the school based-vaccination programme (124). In 2020, boys were also offered the HPV vaccination through the school-based vaccination programme. To examine the effects of HPV vaccination, researchers in the team continued to follow the prevalence of genital and oral HPV at the same youth clinic as the one aforementioned. Already since 2013-2015 (and also later), it could be shown that the prevalence of HPV of the vaccine types decreased considerably in the genital and oral tracts, particularly of vaccinated youths; however, herd immunity was also observed [for further information, please see the review by Du *et al* (125). HPV vaccination has obviously been very successful and, of note, over the past few years the incidence of cervical cancer has decreased; this is prominent, particularly in younger women in Sweden (126). Further research is required to translate existing data into improved HPV vaccination coverage among adolescents.

10. Conclusions

The 11th Workshop on Paediatric Virology organised on December 20, 2025 by the IPV based on the island of Euboea in Greece met its objective of bringing together clinicians and scientists to advance this critical subspecialty in order to shape the future of child healthcare by addressing virology and interactions with a number of disciplines including virology, history of science, bacteriology, neurology imaging, immunology, diabetology, hepatology, paediatrics and maternal health.

The history of smallpox vaccination clearly illustrated the value of knowledge interchange at multiple levels, including folklore medicine providing a foundation for scientific innovation. By sharing observations and techniques across borders, humanity transitioned from dangerous traditional remedies to the first modern vaccines. Gratitude should be paid to the unacknowledged founding Greek fathers of vaccinology, Dr Emmanuel Timonis and Dr Jacob Pylarinos. By studying viral-bacterial interaction, two critical disciplines virology and bacteriology can be bridged. This cross-disciplinary research reveals how viruses exploit bacteria for stability and cellular entry, and how viral infections trigger opportunistic bacterial diseases, through synergistic mechanisms, including viral-mediated epithelial damage, upregulation of bacterial receptors, and immune dysregulation.

The importance of public health and surveillance in paediatric disease has been a valuable lesson taught by the COVID-19 pandemic. The COVID-19 pandemic and its associated NPIs drastically reshaped global disease patterns. Lockdowns, physical distancing, mask mandates, and travel restrictions induced a historic drop in common airborne pathogens (influenza, RSV) and associated secondary bacterial infections, while also causing significant reductions in routine immunisations for other infections. The lifting of the NPIs in the post-COVID 19 era resulted in resurgence of many paediatric infections. The post-COVID era highlighted that robust, active surveillance is critical to managing paediatric infectious diseases.

Neurodevelopment in the foetus and during childhood is vital in ensuring a healthy population of children. Maternal viral infections can affect the neurodevelopment of the foetus; thus, it is important that viral infections in pregnant women are monitored and prevented, to protect foetus from long-term neurological complications, cognitive impairments, and increased risk of neurodevelopmental disorders. HAdVs have been implicated in CNS complications, such as encephalitis and meningoencephalitis, particularly in immunocompromised children, highlighting the importance of a robust immune system in ensuring neurological sequelae following paediatric viral infections. The crossroads of virology, neurology, maternal health, diagnostic imaging technology and immunology were aptly illustrated.

Viral infections have been well-studied and associated as the most common trigger factors of autoimmune conditions in general and T1D in particular, further supporting the requirement for an intact, well-functioning immune system. CVB has been implicated as being diabetogenic and there is a call to develop both preventative vaccines and antiviral therapy to interrupt the virus-to-autoimmunity course of T1D following CVB infection. The importance of the development of both preventative and antiviral modalities was further emphasized by the importance of the HBV vaccine in preventing not only HBV, but also HDV infection and the ultimate development of hepatocellular carcinoma. HPV vaccination can be further promoted within the school-based-vaccination programme.

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References

1. Samuel A and Durning SJ: From crisis to opportunity: Reinventing medical education after COVID-19. Perspect Med Educ 14: 371-382, 2025.
2. Zhao Y, Sun T, Zhang X, Wang X and Hu W: The evolution of medical education in the era of Covid-19 and beyond: A longitudinal study. BMC Med Educ 24: 1289, 2024.
3. Ortiz Riofrio AG, Valdivieso-Andrade EJ, Acosta Masaquiza NM, Aguirre AS, Almeida Villavicencio NA, Calderón Pilla CS, Del Pozo Acosta P, Guaillas Japón A, Luna Chonata DV, Mafla Roca NB, *et al*: COVID-19: Medical education from the point of view of medical students using the participatory Delphi method. PLos One 19: e0297602, 2024.
4. Alrumi N: The impact of COVID-19 on medical education and training. Br J Hosp Med (Lond) 85: 1-7, 2024.
5. Papapanou M, Routsi E, Tsamakis K, Fotis L, Marinos G, Lidoriki I, Karamanou M, Papaioannou TG, Tsiptsios D, Smyrnis N, *et al*: Medical education challenges and innovations during the COVID-19 pandemic. Postgrad Med J 98: 321-327, 2022.
6. Mammas IN, Greenough A, Theodoridou M and Spandidos DA: The foundation of the institute of paediatric virology on the island of Euboea, Greece (review). Exp Ther Med 20: 302, 2020.
7. Mammas IN, Agrafiotis M, Kazani A, Koutsaftiki C, Papatheodoropoulou A, Drysdale SB, Theodoridou M and Spandidos DA: Key lessons from the COVID-19 pandemic: Role of intensive care, politics and science communication (review). Med Int (Lond) 5: 60, 2025.
8. Lau TCW: Toward an immunological turn in nineteenth-century studies. Lit Compass 21: e12707, 2024.
9. Dinc G and Ulman YI: The introduction of variolation 'A La Turca' to the West by Lady Mary Montagu and Turkey's contribution to this. Vaccine 25: 4261-4265, 2007.
10. Eriksen A: Smallpox inoculation: Translation, transference and transformation. Palgrave Commun 52: 1-9, 2020.
11. Timonius E: An account, or history, of the procuring the smallpox by incision, or inoculation; as it has for some time been practised at Constantinople. Phil Trans R Soc Lond 29: 72-82, 1714.
12. Pylarinos J: Nova & tuta vaiolas excitandi per transplantationem methodus, nuper inventa & in usum tracta. Phil Trans R Soc Lond 29: 393-399, 1716.
13. Tucci U: Jacopo Pilarino pioniere dell'innesto del vaiolo. Thesaurismata 37: 421-434, 2007.
14. Poulakou-Rebelakou E and Lascaratos J: Emmanuel timonius, jacobus pylarinus and inoculation. J Med Biogr 11: 181-182, 2003.
15. Berti L: Early reception of smallpox inoculation in Italy: Insights from the correspondence of the fellows of the royal society. Diciottesimo Secolo 6: 5-18, 2021.
16. Kyrkoudis T, Tsoucalas G, Thomaidis V, Bakirtzis I, Nalbanti E, Polychronidis A and Fiska A: Vaccination of the ethnic Greeks (Rums) against smallpox in the ottoman empire: Emmanuel timonis and jacobus pylarinos as precursors of edward jenner. J Clin Pract Res 43: 100-106, 2021.
17. Meyer VN: Innovations from the Levant: Smallpox inoculation and perceptions of scientific medicine. Br J Hist Sci 55: 423-444, 2022.
18. Sharif F: Smallpox inoculation in the Ottoman sultanate: A gendered study of women's involvement in early modern public health. J Br Isl Med Assoc 16: 1-7, 2024.
19. Montagu MW: The Turkish Embassy Letters. Jack M (ed). Virago, London, pp81, 1994.
20. Motraye A: Travels through Europe, Asia, and into part of Africa. London, 2: 396, 1723.
21. Herrera AL, Huber VC and Chaussee MS: The association between invasive group A streptococcal diseases and viral respiratory tract infections. Front Microbiol 7: 342, 2016.
22. Herrera AL, Potts R, Huber VC and Chaussee MS: Influenza enhances host susceptibility to non-pulmonary invasive *Streptococcus pyogenes* infections. Virulence 14: 2265063, 2023.
23. de Gier B, Vlaminckx BJM, Woudt SHS, van Sorge NM and van Asten L: Associations between common respiratory viruses and invasive group A streptococcal infection: A time-series analysis. Influenza Other Respir Viruses 13: 453-458, 2019.
24. Short KR, Kasper J, van der Aa S, Andeweg AC, Zaaraoui-Boutahar F, Goeijenbier M, Richard M, Herold S, Becker C, Scott DP, *et al*: Influenza virus damages the alveolar barrier by disrupting epithelial cell tight junctions. Eur Respir J 47: 954-966, 2016.
25. Mehta D, Petes C, Gee K and Basta S: The role of virus infection in deregulating the cytokine response to secondary bacterial infection. J Interferon Cytokine Res 35: 925-934, 2015.
26. Smallcombe CC, Linfield DT, Harford TJ, Bokun V, Ivanov AI, Piedimonte G and Rezaee F: Disruption of the airway epithelial barrier in a murine model of respiratory syncytial virus infection. Am J Physiol Lung Cell Mol Physiol 316: L358-L368, 2019.
27. Abo YN, Oliver J, McMinn A, Osowicki J, Baker C, Clark JE, Blyth CC, Francis JR, Carr J, Smeesters PR, *et al*: Increase in invasive group A streptococcal disease among Australian children coinciding with northern hemisphere surges. Lancet Reg Health West Pac 41: 100873, 2023.
28. de Gier B, van de Kassteele J, van Asten L, Schoffelen AF; ISIS-AR study group; Hooiveld M, Te Wierik MJ, van Sorge NM and de Melker HE; Members of the ISIS-AR study group: Attribution of invasive group A streptococcal infections (iGAS) to predisposing viral infections, the Netherlands, 2010 to 2023. Euro Surveill 29: 2300739, 2024.
29. Laing KL, Ouwendijk WJD, Koelle DM and Verjans GMGM: Immunobiology of varicella-zoster virus infection. J Infect Dis 218 (Suppl 2): S68-S74, 2018.
30. Cohen R, Ashman M, Taha MK, Varon E, Angoulvant F, Levy C, Rybak A, Ouldali N, Guiso N and Grimprel E: Pediatric infectious disease group (GPIP) position paper on the immune debt of the COVID-19 pandemic in childhood, how can we fill the immunity gap? Infect Dis Now 51: 418-423, 2021.
31. Lenglart L, Titomanlio L, Bognar Z, Bressan S, Buonsenso D, De T, Farrugia R, Honeyford K, Maconochie IK, Moll HA, *et al*: Surge of pediatric respiratory tract infections after the COVID-19 pandemic and the concept of 'immune debt'. J Pediatr 284: 114420, 2024.
32. Rubin R: From 'immunity debt' to 'immunity theft'-How COVID-19 might be tied to recent respiratory disease surges. JAMA 331: 378-381, 2024.
33. Nygaard U, Holm M, Rabie H and Rytter M: The pattern of childhood infections during and after the COVID-19 pandemic. Lancet Child Adolesc Health 8: 910-920, 2024.
34. Esposito S, Masetti M, Calanca C, Canducci N, Rasmi S, Fradusco A and Principi N: Recent changes in the epidemiology of group A streptococcus infections: Observations and implications. Microorganisms 13: 1871, 2025.
35. Dokal K, Channon-Wells S, Davis C, Estrada-Rivadeneyra D, Huse KK, Lias A, Hamilton S, Guy RL, Lamagni T, Nichols S, *et al*: Immunity to Streptococcus pyogenes and common respiratory viruses at age 0-4 years after COVID-19 restrictions. JAMA Netw Open 8: e2537808, 2025.
36. Centers for Disease Control and Prevention: Increase in invasive group A strep infections, 2022-2023. Available from: https://www.cdc.gov. Assessed at February 2, 2023.
37. European Centre for Disease Prevention and Control: Increase in Invasive Group A Streptococcal infections among children in Europe, including fatalities. Available from: https://www.ecdc.europa.eu/en/news-events/increase-invasive-group-streptococcal-infections-among-children-europe-including. Assessed at December 12, 2022.
38. World Health Organization: Increased incidence of scarlet fever and invasive group A Streptococcus infection-multi-country. Available from: https://www.who.int. Assessed at December 15, 2022.
39. Dabaja-Younis H, Kandel C, Green K, Johnstone J, Zhong Z, Kassee C, Allen V, Armstrong I, Baqi M, Barker K, *et al*: Invasive group A Streptococcal infection in children, 1992-2023. JAMA Netw Open 8: e252861, 2025.

40. Fafi I, Assad Z, Lenglart L, Valtuille Z, Kaguelidou F, Aupiais C, Bourmaud A, Rybak A, Bechet S, Levy C, *et al*: Did the resurgence of childhood lower respiratory infections offset the initial benefit of COVID-19-related non-pharmaceutical interventions in children? A time-series analysis. BMC Med 23: 66, 2025.
41. Tomidis Chatzimanouil MK, Rößler S, Nurjadi D, Iakovidis I, Berner R, Toepfner N, Bornstein TDGASSGSR, Aschoff R, Bornhäuser M, Güldner A, *et al*: Post-COVID-19-pandemic changes and clinical characteristics of invasive group a streptococcal infections from 2015 to 2023. Infection 53: 991-1000, 2025.
42. Papaioannou G and Garel C: The fetal brain: Migration and gyration anomalies-pre- and postnatal correlations. Pediatr Radiol 53: 589-601, 2023.
43. Abou-Ismail MY, Diamond A, Kapoor S, Arafah Y and Nayak L: The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. Thromb Res 194: 101-115, 2020.
44. Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A, Kneen R, Defres S, Sejvar J and Solomon T: Neurological associations of COVID-19. Lancet Neurol 19: 767-783, 2020.
45. Papaioannou G, Klein W, Cassart M and Garel C: Indications for magnetic resonance imaging of the fetal central nervous system: Recommendations from the European society of paediatric radiology fetal task force. Pediatr Radiol 51: 2105-2114, 2021.
46. Kienast P, Prayer D, Binder J, Prayer F, Dekan S, Langthaler E, Sigl B, Eichinger S, Perkmann-Nagele N, Stuempflen I, *et al*: SARS-CoV-2 variant-related abnormalities detected by prenatal MRI: A prospective case-control study. Lancet Reg Health Eur 26: 100587, 2023.
47. Mappa I, Pietrolucci ME, Pavjola M, Maruotti G, D'Antonio F and Rizzo G: Fetal brain biometry and cortical development after maternal SARS-CoV-2 infection in pregnancy: A prospective case-control study. J Clin Ultrasound 51: 639-643, 2023.
48. Andescavage N, Lu YC, Wu Y, Kapse K, Keller J, Von Kohorn I, Afifi A, Vezina G, Henderson D, Wessel DL, *et al*: Intrauterine exposure to SARS-CoV-2 infection and early newborn brain development. Cereb Cortex 34: bhae041, 2024.
49. Rajagopalan V, Reynolds WT, Zepeda J, Lopez J, Ponrartana S, Wood J, Ceschin R and Panigrahy A: Impact of COVID-19-related maternal stress on fetal brain development: A multimodal MRI study. J Clin Med 11: 6635, 2022.
50. Schwartz DA, Avvad-Portari E, Babál P, Baldewijns M, Blomber M, Bouachba A, Camacho J, Collardeau-Frachon S, Colson A, Dehaene I, *et al*: Placental tissue destruction and insufficiency from COVID-19 causes stillbirth and neonatal death from hypoxic-ischemic injury. Arch Pathol Lab Med 146: 660-676, 2022.
51. Manti S, Spoto G, Nicoreta AG, Di Rosa G and Piedimonte G: Impact of respiratory viral infections during pregnancy on the neurological outcomes of the newborn: Current knowledge. Front Neurosci 17: 1320319, 2024.
52. Vivanti AJ, Vauloup-Fellous C, Prevot S, Zupan V, Suffee C, Do Cao J, Benachi A and De Luca D: Transplacental transmission of SARS-CoV-2 infection. Nat Commun 11: 3572, 2020.
53. Alves de Araujo Junior D, Motta F, Fernandes GM, Castro MEC, Sasaki LMP, Luna LP, Rodrigues TS, Kurizky PS, Soares AASM, Nobrega OT, *et al*: Neuroimaging assessment of pediatric cerebral changes associated with SARS-CoV-2 infection during pregnancy. Front Pediatr 11: 1194114, 2023.
54. Cherry JD and Chen TK: Chapter 168-Adenovirus. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases. Feigin RD, Cherry JD, Demmler-Harrison GJ and Kaplan SL (eds). 6th edition. W.B. Saunders, Philadelphia, pp1949-1972, 2009.
55. Mammas IN, Drysdale SB, Charalampous C, Koletsi P, Papatheodoropoulou A, Koutsaftiki C, Sergentanis T, Merakou K, Kornarou H, Papaioannou G, *et al*: Navigating paediatric virology through the COVID 19 era (review). Int J Mol Med 52: 83, 2023.
56. Abu-Helalah M, Al-Hanaktah M, Abu Lubad M, Al Tibi A, Alhousani M and Drysdale SB: The epidemiology and clinical burden of human adenovirus respiratory infections among hospitalized children under 5 years in Jordan. Pediatr Infect Dis J 45: 229-235, 2026.
57. World Health Organization (WHO): Severe acute hepatitis of unknown aetiology in children-Multi-country (12 July 2022). Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON400. Assessed at July 22, 2022.
58. Sakrani N, Almazrouei S, Mohan S and Ramsi M: Adenovirus as a rare cause of acute necrotising encephalitis. BMJ Case Rep 12: e232338, 2019.
59. Mizuno S, Tanimoto Y, Mori A, Fuseya T, Ishida Y, Nishiyama M, Maruyama A and Kasai M: Acute encephalopathy associated with human adenovirus type 14 infection in 7-year-old girl, Japan. Emerg Infect Dis 31: 377-379, 2025.
60. Reyes-Andrade J, Sánchez-Céspedes J, Olbrich P, Falcon L, Sanchez-Ganfornina I, Tebruegge M, Pérez-Romero P and Neth O: Meningoencephalitis due to adenovirus in a healthy infant mimicking severe bacterial sepsis. Pediatr Infect Dis J 33: 416-419, 2014.
61. Zhao H, Liu Y, Feng Z, Feng Q, Li K, Gao H, Qian S, Xu L and Xie Z: A fatal case of viral sepsis and encephalitis in a child caused by human adenovirus type 7 infection. Virol J 19: 154, 2022.
62. Straussberg R, Harel L, Levy Y and Amir J: A syndrome of transient encephalopathy associated with adenovirus infection. Pediatrics 107: E69, 2001.
63. Schwartz KL, Richardson SE, MacGregor D, Mahant S, Raghuram K and Bitnun A. Adenovirus-associated central nervous system disease in children. J Pediatr 205: 130-137, 2019.
64. Huang YC, Huang SL, Chen SP, Huang YL, Huang CG, Tsao KC and Lin TY: Adenovirus infection associated with central nervous system dysfunction in children. J Clin Virol 57: 300-304, 2013.
65. Vidal LR, de Almeida SM, Cavalli BM, Dieckmann TG, Raboni SM, Salvador GLO, Pereira LA, Rotta I and Nogueira MB: Human adenovirus meningoencephalitis: A 3-years' overview. J Neurovirol 25: 589-596, 2019.
66. Tian J, Wang X, Zhang L, Li Q, Feng G, Zeng Y, Wang R and Xie Z: Clinical epidemiology and disease burden of adenoviral encephalitis in hospitalized children in China: A nationwide cross-sectional study. Pediatr Investig 7: 247-253, 2023.
67. Zhang XF, Tan CB, Yao ZX, Jiang L and Hong SQ: Adenovirus infection-associated central nervous system disease in children. Pediatr Infect Dis J 40: 205-208, 2021.
68. Koskiniemi M, Korppi M, Mustonen K, Rantala H, Muttilainen M, Herrgård E, Ukkonen P and Vaheri A: Epidemiology of encephalitis in children. A prospective multicentre study. Eur J Pediatr 156: 541-545, 1997.
69. Alcamo AM, Wolf MS, Alessi LJ, Chong HJ, Green M, Williams JV and Simon DW: Successful use of cidofovir in an immunocompetent child with severe adenoviral sepsis. Pediatrics 145: e20191632, 2020.
70. Leen AM, Bollard CM, Mendizabal AM, Shpall EJ, Szabolcs P, Antin JH, Kapoor N, Pai SY, Rowley SD, Kebriaei P, *et al*: Multicenter study of banked third-party virus-specific T cells to treat severe viral infections after hematopoietic stem cell transplantation. Blood 121: 5113-5123, 2013.
71. Ullah S, Zheng Z, Rahman W, Ullah F, Ullah A, Iqbal MN, Iqbal N and Gao T: A computational approach to fighting type 1 diabetes by targeting 2C Coxsackie B virus protein with flavonoids. PLoS One 18: e0290576, 2023.
72. Dahl-Jørgensen K: Virus as the cause of type 1 diabetes. Trends Mol Med 30: 1020-1027, 2024.
73. Stene LC, Oikarinen S, Hyöty H, Barriga KJ, Norris JM, Klingensmith G, Hutton JC, Erlich HA, Eisenbarth GS and Rewers M: Enterovirus infection and progression from islet autoimmunity to type 1 diabetes: The diabetes and autoimmunity study in the young (DAISY). Diabetes 59: 3174-3180, 2010.
74. Hyoty H, Leon F and Knip M: Developing a vaccine for type 1 diabetes by targeting coxsackievirus B. Expert Rev Vaccines 17: 1071-1083, 2018.
75. Harris HF: A case of diabetes mellitus quickly following mumps-on the pathological alterations of the salivary glands, closely resembling those found in the pancreas, in a case of diabetes mellitus. Boston Med Surg J 140: 465-469, 1899.
76. Jeremiah SS, Moin ASM and Butler AE: Virus-induced diabetes mellitus: Revisiting infection etiology in light of SARS-CoV-2. Metabolism 156: 155917, 2014.
77. Amin A, Rasheed MA, Diwan RA, Shahid M, Bano S, Riaz A, Iqbal MN and Sajid MW: Inhibition of 2C coxsackie B virus protein to decrease pathogenicity of diabetes mellitus type 1. Curr Comput Aided Drug Des 16: 318-326, 2020.
78. Hankaniemi MM, Laitinen OH, Stone VM, Sioofy-Khojine A, Määttä JAE, Larsson PG, Marjomäki V, Hyöty H, Flodström-Tullberg M and Hytönen VP: Optimized production and purification of Coxsackievirus B1 vaccine and its preclinical evaluation in a mouse model. Vaccine 35: 3718-3725, 2017.

79. Stone VM, Hankaniemi MM, Svedin E, Sioofy-Khojine A, Oikarinen S, Hyöty H, Laitinen OH, Hytönen VP and Flodström-Tullberg M: A Coxsackievirus B vaccine protects against virus-induced diabetes in an experimental mouse model of type 1 diabetes. Diabetologia 61: 476-481, 2018.
80. Yin H, Berg AK, Tuvemo T and Frisk G: Enterovirus RNA is found in peripheral blood mononuclear cells in a majority of type 1 diabetic children at onset. Diabetes 51: 1964-1971, 2002.
81. Krogvold L, Mynarek IM, Ponzi E, Mørk FB, Hessel TW, Roald T, Lindblom N, Westman J, Barker P, Hyöty H, *et al*: Pleconaril and ribavirin in new-onset type 1 diabetes: A phase 2 randomized trial. Nat Med 29: 2902-2908, 2023.
82. Greenbaum CJ, Lord S and Speake C: Type 1 diabetes mellitus: Pathophysiology and etiology. Hirsch IB (ed). UpToDate, Wolters Kluwer, 2026.
83. Hyöty H, Kääriäinen S, Laiho JE, Comer GM, Tian W, Härkönen T, Lehtonen JP, Oikarinen S, Puustinen L, Snyder M, *et al*: Safety, tolerability and immunogenicity of PRV-101, a multivalent vaccine targeting coxsackie B viruses (CVBs) associated with type 1 diabetes: A double-blind randomised placebo-controlled phase I trial. Diabetologia 67: 811-821, 2024.
84. Maggiore G, Hadchouel M, Sessa F, Vinci M, Craxi A, Marzani MD, De Giacomo C and Alagille D: A retrospective study of the role of delta agent infection in children with HBsAg-positive chronic hepatitis. Hepatology 5: 7-9, 1985.
85. Abbas Z, Soomro GB, Hassan SM and Luck NH: Clinical presentation of hepatitis D in Pakistani children. Eur J Gastroenterol Hepatol 26: 1098-1103, 2014.
86. Manesis EK, Vourli G, Dalekos G, Vasiliadis T, Manolaki N, Hounta A, Koutsounas S, Vafiadis I, Nikolopoulou G, Giannoulis G, *et al*: Prevalence and clinical course of hepatitis delta infection in Greece: A 13-year prospective study. J Hepatol 59: 949-956, 2013.
87. Karagas MR, Kaldor J, Michaelis M, Muchengeti MM, Alfaiate D, Argirion I, Chen X, Cunha C, Hantz S, Koljonen V, *et al*: Carcinogenicity of hepatitis D virus, human cytomegalovirus, and Merkel cell polyomavirus. Lancet Oncol: Jun 26, 2025 (Epub ahead of print).
88. Kramvis A, Mammas IN and Spandidos DA: Exploring the optimal vaccination strategy against hepatitis B virus in childhood (review). Biomed Rep 19: 48, 2023.
89. Caviglia GP, Ciancio A and Rizzetto M: A Review of HDV infection. Viruses 14: 1749, 2022.
90. Stockdale AJ, Kreuels B, Henrion MYR, Giorgi E, Kyomuhangi I, de Martel C, Hutin Y and Geretti AM: The global prevalence of hepatitis D virus infection: Systematic review and meta-analysis. J Hepatol 73: 523-532, 2020.
91. Polaris Observatory Collaborators: Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: A modelling study. Lancet Gastroenterol Hepatol 3: 383-403, 2018.
92. Stockdale AJ, Chaponda M, Beloukas A, Phillips RO, Matthews PC, Papadimitropoulos A, King S, Bonnett L and Geretti AM: Prevalence of hepatitis D virus infection in sub-Saharan Africa: A systematic review and meta-analysis. Lancet Glob Health 5: e992-e1003, 2017.
93. Kasatkina L, Fedorchenko V, Sidorova I, Gomenyuk L, Yakovets O, Brandl M, Ivanchuk I, Dudareva S and Nesterova O: National representative seroprevalence of viral hepatitis B, C, and D seromarkers in Ukraine, 2021. Euro Surveill 30: 2500015, 2025.
94. AlNaamani KM, Al-Tamtami W, El-Kassas M, Omar H, AlKalbani A, Kamath BR, Alshuaili H, Anwar A, AlKalbani A, AlShukaili H, *et al*: The seroprevalence, risk factors, and clinical profile of hepatitis D in Omani patients with chronic hepatitis B: A multicenter cross-sectional study. J Clin Med 14: 7089, 2025.
95. Tsaneva-Damyanova DT and Georgieva LH: Epidemiology pattern, prevalent genotype distribution, fighting stigma and control options for hepatitis D in Bulgaria and other European countries. Life (Basel) 13: 1115, 2023.
96. Cabezas C, Trujillo O, Balbuena J, Peceros FM, Terrazas M, Suárez M, Marin L, Apac J and Ramírez-Soto MC: Decrease in the prevalence of hepatitis B and D virus infections in an endemic area in Peru 23 years after the introduction of the first pilot vaccination program against hepatitis B. PLoS One 15: e0236993, 2020.
97. Pisaturo M, Alessio L, Di Fraia A, Macera M, Minichini C, Cordua E, Onorato L, Scotto G, Di Caprio G, Calò F, *et al*: Hepatitis D virus infection in a large cohort of immigrants in southern Italy: A multicenter, prospective study. Infection 50: 1565-1572, 2022.
98. Ordieres C, Navascués CA, González-Diéguez ML, Rodríguez M, Cadahía V, Varela M, Rodrigo L and Rodríguez M: Prevalence and epidemiology of hepatitis D among patients with chronic hepatitis B virus infection: A report from northern Spain. Eur J Gastroenterol Hepatol 29: 277-283, 2017.
99. El Bouzidi K, Elamin W, Kranzer K, Irish DN, Ferns B, Kennedy P, Rosenberg W, Dusheiko G, Sabin CA, Smith BC and Nastouli E: Hepatitis delta virus testing, epidemiology and management: A multicentre cross-sectional study of patients in London. J Clin Virol 66: 33-37, 2015.
100. Ducancelle A, Abgueguen P, Birguel J, Mansour W, Pivert A, Le Guillou-Guillemette H, Sobnangou JJ, Rameau A, Huraux JM and Lunel-Fabiani F: High endemicity and low molecular diversity of hepatitis B virus infections in pregnant women in a rural district of north Cameroon. PLoS One 8: e80346, 2013.
101. Torimiro JN, Nanfack A, Takang W, Keou CK, Joyce AN, Njefi K, Agyingi K, Domkam I, Takou D, Moudourou S, *et al*: Rates of HBV, HCV, HDV and HIV type 1 among pregnant women and HIV type 1 drug resistance-associated mutations in breastfeeding women on antiretroviral therapy. BMC Pregnancy Childbirth 18: 504, 2018.
102. Ndzie Ondigui JL, Mafopa Goumkwa N, Lobe C, Wandji B, Awoumou P, Voussou Djivida P, Peyonga P, Manju Atah S, Verbe V, Kamgaing Simo R, *et al*: Prevalence and risk factors of transmission of hepatitis delta virus in pregnant women in the Center Region of Cameroon. PLoS One 19: e0287491, 2024.
103. Terrault NA, Levy MT, Cheung KW and Jourdain G: Viral hepatitis and pregnancy. Nat Rev Gastroenterol Hepatol 18: 117-130, 2021.
104. Sellier PO, Maylin S, Brichler S, Bercot B, Lopes A, Chopin D, Pogliaghi M, Munier AL, Delcey V, Simoneau G, *et al*: Hepatitis B virus-hepatitis D virus mother-to-child co-transmission: A retrospective study in a developed country. Liver Int 38: 611-618, 2018.
105. Chilaka VN and Konje JC: Viral hepatitis in pregnancy. Eur J Obstet Gynecol Reprod Biol 256: 287-296, 2021.
106. Yang S, Zhong L, Huang L, Lin S and Li Y: Global burden and trends of viral hepatitis among women of childbearing age from 1990 to 2021. Front Microbiol 16: 1553129, 2025.
107. European Association for the Study of the Liver: EASL 2017 clinical practice guidelines on the management of hepatitis B virus infection. J Hepatol 67: 370-398, 2017.
108. Bardak AE, Ozturk NB, Gurakar M, Sequeira L, Yildiz E, Ozmert EH, Idilman R and Gurakar A: Updates on recent advancements in hepatitis D virus treatment. Viruses 17: 1100, 2025.
109. Vanwolleghem T, Armstrong PA, Buti M, FitzSimons D, Valckx S, Hendrickx G and Van Damme P: The elimination of hepatitis D as a public health problem: Needs and challenges. J Viral Hepat 31: 47-50, 2024.
110. Tommasino M: The human papillomavirus family and its role in carcinogenesis. Semin Cancer Biol 26: 13-21, 2014.
111. Schiller JT and Lowy DR: Papillomavirus-like particles and HPV vaccine development. Semin Cancer Biol 7: 373-382, 1996.
112. Schiller J and Lowy D: Explanations for the high potency of HPV prophylactic vaccines. Vaccine 36: 4768-4773, 2018.
113. International Agency for Research on Cancer: IARC monographs on the evaluation of carcinogenic risks to humans. Volume 64, Human papillomaviruses. Lyon, France, 1995.
114. Mellin H, Friesland S, Lewensohn R, Dalianis T and Munck-Wikland E: Human papillomavirus (HPV) DNA in tonsillar cancer: Clinical correlates, risk of relapse, and survival. Int J Cancer 89: 300-304, 2000.
115. Dahlgren L, Dahlstrand HM, Lindquist D, Högmo A, Björnestål L, Lindholm J, Lundberg B, Dalianis T and Munck-Wikland E: Human papillomavirus is more common in base of tongue than in mobile tongue cancer and is a favorable prognostic factor in base of tongue cancer patients. Int J Cancer 112: 1015-1019, 2004.
116. Hammarstedt L, Lindquist D, Dahlstrand H, Romanitan M, Dahlgren LO, Joneberg J, Creson N, Lindholm J, Ye W, Dalianis T and Munck-Wikland E: Human papillomavirus as a risk factor for the increase in incidence of tonsillar cancer. Int J Cancer 119: 2620-2623, 2006.
117. Näsman A, Attner P, Hammarstedt L, Du J, Eriksson M, Giraud G, Ahrlund-Richter S, Marklund L, Romanitan M, Lindquist D, *et al*: Incidence of human papillomavirus (HPV) positive tonsillar carcinoma in Stockholm, Sweden: An epidemic of viral-induced carcinoma? Int J Cancer 125: 362-366, 2009.

118. Attner P, Du J, Näsman A, Hammarstedt L, Ramqvist T, Lindholm J, Marklund L, Dalianis T and Munck-Wikland E: The role of human papillomavirus in the increased incidence of base of tongue cancer. Int J Cancer 126: 2879-2884, 2010.
119. Sturgis EM and Cinciripini PM: Trends in head and neck cancer incidence in relation to smoking prevalence: An emerging epidemic of human papillomavirus-associated cancers? Cancer 110: 1429-1435, 2007.
120. Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, Jiang B, Goodman MT, Sibug-Saber M, Cozen W, *et al*: Human papillomavirus and rising oropharyngeal cancer incidence in the United States. J Clin Oncol 29: 4294-4301, 2011.
121. Ramqvist T, Du J, Lundén M, Ahrlund-Richter S, Ferreira J, Marions L, Sparén P, Andersson S and Dalianis T: Pre-vaccination prevalence of human papillomavirus types in the genital tract of 15-23-year-old women attending a youth health clinic in Stockholm, Sweden. Scand J Infect Dis 43: 115-121, 2011.
122. Du J, Nordfors C, Ahrlund-Richter A, Sobkowiak M, Romanitan M, Näsman A, Andersson S, Ramqvist T and Dalianis T: Prevalence of oral human papillomavirus infection among youth, Sweden. Emerg Infect Dis 18: 1468-1471, 2012.
123. Nordfors C, Grün N, Haeggblom L, Tertipis N, Sivars L, Mattebo M, Larsson M, Häggström-Nordin E, Tydén T, Ramqvist T and Dalianis T: Oral human papillomavirus prevalence in high school students of one municipality in Sweden. Scand J Infect Dis 45: 878-881, 2013.
124. Tegnell A, Dillner J and Andrae B: Introduction of human papillomavirus (HPV) vaccination in Sweden. Euro Surveill 14: 19119, 2009.
125. Du J, Ährlund-Richter A, Näsman A and Dalianis T: Human papilloma virus (HPV) prevalence upon HPV vaccination in Swedish youth: A review based on our findings 2008-2018, and perspectives on cancer prevention. Arch Gynecol Obstet 303: 329-335, 2021.
126. Statistics from the Swedish Cancer Registry 1970-2024. Available from: https://sdb.socialstyrelsen.se/if_can/resultat.aspx. Assessed at December 4, 2025.