



World Health
Organization



Why encephalitis matters?

Report of the virtual meeting

28-29 June 2022

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The findings and conclusions of this report are those of the participants and do not necessarily represent the official position of their organizations.

Abbreviations and acronyms

CNS	central nervous system
CSF	cerebrospinal fluid
DALY	disability-adjusted life year
HIV	human immunodeficiency virus
HSV	herpes simplex virus
IV	intravenous
JE	Japanese encephalitis
LMIC	low- and middle-income countries
LP	lumbar puncture
MRI	magnetic resonance imaging
NIHR	National Institute for Health and Social Care Research
NIMHANS	National Institute of Mental Health and Neurosciences
PCR	polymerase chain reaction
PEP	post-exposure prophylaxis
RIG	rabies immunoglobulin
TBE	tick-borne encephalitis
United Kingdom	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
VZV	varicella-zoster virus
WHO	World Health Organization

Executive summary

Neurological disorders, including encephalitis, are the leading cause of disability-adjusted life years (DALYs) and second leading cause of death worldwide.

Encephalitis has a significant impact on individuals across the lifespan, and on families, communities and societies. Almost half a million people globally were thought to have developed acute encephalitis in 2019; however, that figure is considered an underestimate. Encephalitis is a growing global threat because of increased population density in underresourced communities, intensive farming practices, vaccine hesitancy, the increasing identification of autoimmune causes, and climate change. Social factors such as low socioeconomic status increase the risk for rabies transmission in dog populations. There is also a significant risk of outbreaks associated with emerging and re-emerging viral causes of encephalitis.

The cost and global burden of encephalitis on people affected, their families and society is currently unknown – particularly in low- and middle-income countries (LMIC). However, the heavy costs associated with neurological sequelae and the impact on families are thought to be similar to those associated with other central nervous system infections such as meningitis.

In May 2022, the *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031* was adopted by the 75th World Health Assembly. Other World Health Organization (WHO) initiatives relevant to encephalitis include Defeating meningitis by 2030, a global roadmap; universal health coverage; the One Health approach to addressing zoonotic diseases; the Global Vaccine Action Plan; the Global vector control response 2017-2030; the Global framework for multi-disease elimination; the Global Arbovirus Initiative and programmes related to pathogen-specific WHO initiatives (e.g. Japanese encephalitis, tick-borne encephalitis, measles, rabies and varicella-zoster virus). It is important to consider encephalitis in the context of the *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031* and other initiatives.



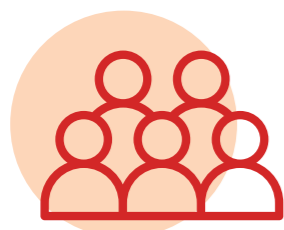
Encephalitis has a significant impact on individuals across the lifespan, and on families, communities and societies

The “Encephalitis as a public health priority” virtual meeting aimed to discuss mechanisms to strengthen countries’ capacity to respond to the public health challenge posed by encephalitis and reduce the burden faced by individuals, families, communities and societies.

Objectives

The objectives of the meeting were to:

- review, discuss and share experiences to address the public health aspects of encephalitis including diagnosis, treatment and care, prevention, support for people with encephalitis and their carers, and advocacy and awareness; and
- identify mechanisms to strengthen countries’ capacity to respond to the public health challenge posed by encephalitis, with an emphasis on LMIC.



42

participants were brought together by the WHO “Encephalitis as a public health priority” virtual meeting

Outcomes

The WHO virtual meeting brought together 42 participants, including service providers, academics, researchers, civil society representatives, people with lived experience and carers, to discuss mechanisms to strengthen countries’ capacity to respond to the public health challenge posed by encephalitis, with an emphasis on LMIC.

On Day 1 of the meeting, the stage was set with presentations about policy contexts, the global burden of encephalitis and challenges faced. Participants presented and discussed diagnostics, treatment and care; they also heard the voices and perspectives of people with encephalitis and their carers. On Day 2, participants shared experiences about prevention, surveillance, research and support for people with encephalitis and their families.



The main themes emerging from the meeting were the need for:

- information on the burden of encephalitis, including health economics data particularly in LMIC; better understanding of the severity of the disease (including disability and mortality); and strengthening routine health information systems;
- advocacy and awareness, including addressing stigma and discrimination and emphasizing the important role of people with encephalitis, their families and civil society organizations;
- improved diagnosis, public awareness and education materials for better diagnosis and care (including better support for rehabilitation);
- better treatment and care, including education and training of health care providers, integrated care across the continuum of services through universal health coverage, multidisciplinary care and improved access to affordable first-line medications;
- improved management of sequelae, including neurocognitive impairment, seizures and psychiatric symptoms;
- prevention, including advocacy for vaccines, integration of vaccines into national programmes, and vaccine education through primary care and community leaders;
- research and surveillance, including different types of surveillance, an encephalitis case definition that balances sensitivity and specificity, diagnostics with surveillance and globally harmonized surveillance (including sentinel surveillance sites with enhanced diagnostics); and
- support for people with encephalitis and their carers, including recognition of strategies to reduce carer burden including support, learning from other conditions and managing disinformation.

Introduction

Encephalitis is an inflammation of the brain that is caused by an infection or by host immune responses. More than 100 different causative organisms have been recognized, although often the cause of encephalitis is unknown (1-5). The true incidence of encephalitis is currently unknown and is difficult to estimate owing to inaccurate reporting systems, which include sequelae within incidence measurements.

Encephalitis is a growing global threat owing to increased population density in underresourced communities, intensive farming practices, vaccine hesitancy, the increasing identification of autoimmune causes, outbreaks associated with emerging and re-emerging viral causes of encephalitis and climate change. It has high rates of mortality and morbidity, affects people across the lifespan and results in significant neurological sequelae with long-term consequences to quality of life and wider society.



Encephalitis has high rates of mortality and morbidity and results in significant neurological sequelae

Global challenges

Encephalitis is associated with high mortality on a global scale, with varying case fatality rates reported; for example, 9% for all-cause encephalitis in the United States of America (USA), 20% for Japanese encephalitis (JE) and up to 40% for autoimmune encephalitis (6-8). Surviving individuals often suffer significant sequelae. Neurodevelopmental sequelae such as developmental delay (35%), abnormal behaviour (18%), cognitive impairment (17.5%) and motor impairment (17%) have been reported in a significant proportion of paediatric survivors of encephalitis (9). Between 26% and 62% of adults suffer neurological sequelae, including epilepsy, memory problems, behavioural issues, fatigue or sleep disturbance, personality changes, cognitive impairment, pain and abnormal sensations, motor impairment, movement disorders and challenges with daily living skills. (10-16). Encephalitis is associated with high DALYs, but estimates of DALYs vary depending on the accuracy of the input estimates (i.e. incidence or prevalence, mortality and sequelae). Globally, 4.8 million DALYs related to encephalitis were estimated in 2019 owing to the high burden of subsequent neurological sequelae (17).

Sequelae following encephalitis affect not only the survivor but also families and communities. Caregiving, particularly in neurological diseases, is costly and time-consuming and can increase the risk for depression and worse physical health (18, 19).

Owing to its high morbidity and mortality, encephalitis is associated with significant costs to individuals, the health system and society. Data on the global costs of encephalitis are lacking – particularly in LMIC. Encephalitis-associated hospitalisations in the USA were estimated to cost US\$ 2 billion in 2010 (20). Based only on bed-days of hospital occupancy between 2005 and 2009, an annual cost of more than US\$ 35 million for encephalitis has been estimated in England (21). A study in China focusing on JE alone estimated a total economic burden between 2013 and 2018 of US\$ 12.01 million, with US\$ 8.32 million from direct costs and US\$ 3.69 million due to indirect costs (22). In an LMIC such as Nepal, the median out-of-pocket cost to families is often 5–10 times the median monthly income (23).

In summary, encephalitis presents a significant global disease burden because of the rising incidence and development of long-term neurological sequelae. The disease burden is unequally distributed globally and is often highest in LMIC, where resources are most limited (17). Countries face numerous challenges to address the devastating impact of encephalitis on survivors, families, communities, societies and economies.

Disparities in access to diagnostic tests for encephalitis

Encephalitis is best diagnosed by specialists in neurology or infectious disease; however, there are often delays in diagnosis because of lack of recognition and prompt treatment by primary care providers, community health care workers, traditional healers and the public. Delays in recognition and treatment can severely affect mortality and morbidity – particularly in highly virulent cases such as herpes encephalitis. The WHO Neurology Atlas provides estimates of 0.03 neurologists per 100 000 population in low-income countries and 4.74 per 100 000 population in high-income countries; in 2017, only 23% of countries worldwide had neurologists in rural areas (24). Given this lack of specialized expertise, training primary care providers and other health care workers to recognize the symptoms of encephalitis is imperative.

Cerebrospinal fluid (CSF) remains the specimen of choice to investigate the aetiology of encephalitis and detect the presence of an organism within the central nervous system (CNS). Nevertheless, microbiological tests performed on specimens other than CSF and neuroimaging can provide important supporting diagnostic information in the absence of a lumbar puncture (LP), and such tests may be especially important for certain causes.

The WHO essential diagnostics list (EDL) – recommends in vitro diagnostics that should be available at the point-of-care and in laboratories in all countries to increase timely and life-saving diagnoses. It recommends microscopy and culture of CSF specimens for bacteriology, mycology and parasitology (25, 26). In addition, tests that pertain to neurology include CSF cryptococcal antigen (cryptococcal meningitis), CSF wet mount preparation, CSF nucleic acid amplification test (CNS tuberculosis), CSF venereal disease research laboratory

test (neurosyphilis), CSF cell cytology and CSF biochemistry (25, 26).

The global inequity in the availability of laboratory tests for the aetiological diagnosis of encephalitis is stark. Basic CSF microscopy and culture appear to be available in most countries (27). These tests can generally help with diagnosing nonviral causes of encephalitis; however, most viral or autoimmune cases would require other specialized (i.e. not routinely available) testing. CSF analysis also relies on performance of an LP, but this is not always carried out (28). A current key activity of the WHO Defeating meningitis roadmap is to evaluate reasons for the low frequency of LPs (29). The availability of polymerase chain reaction (PCR) for CSF herpes simplex virus (HSV) varies and it is often lacking in places that need it (30, 31). Diagnosis of HSV encephalitis is important because treatment is available and the outcome is better if treatment is initiated early in the illness. Access to nucleic acid amplification tests remains largely insufficient in LMIC and remains limited to predominantly HIV and tuberculosis (32). Reasons for this situation include lack of basic microbiology laboratories, lack of skilled staff, inability to report results in a timely manner, lack of laboratory accreditation and quality assurance, and clinician preference.

Imaging modalities that could assist with the investigation process are computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) scans, but again their availability is not widespread, with many regions having significant shortages of these technologies. There are far more MRI scanners per million population in high-income countries (19.51/1 000 000) than in lower income countries (2.85, 0.25 and 0.1 per 1 000 000 in upper middle, lower middle and low-income countries, respectively). In Africa, if MRI facilities

are available they are often located in urban areas (mainly capital cities) and accessible only within the private health care sector (33).

Antibody testing for autoimmune encephalitis is available in Europe, North America and Australia. Standardised, commercial diagnostic kits are available for the most common subtypes; however, analysis and interpretation require expensive kits or reagents, training, ongoing quality measures, preanalytic pipelines and sophisticated laboratory equipment, which severely limits their availability in LMIC.

Disparities in access to treatment for encephalitis

Treatment for encephalitis is largely supportive but specific treatment is available for HSV encephalitis, varicella-zoster virus (VZV), and nonviral and immune-mediated causes. In most developed countries, early treatment with intravenous (IV) aciclovir is recommended before making a definitive diagnosis; oral aciclovir is not suitable because it does not result in adequate CSF concentration to achieve antiviral efficacy. Prompt treatment with IV aciclovir has reduced the case fatality rate of HSV encephalitis from 70% to 20% and is also recommended for VZV encephalitis (36, 37). The WHO list of essential medicines includes aciclovir for both adults and children, but does not specify encephalitis or the route of administration (38). Laboratory capacity to adequately monitor renal function is required with IV aciclovir use.

Also, there is a high degree of heterogeneity among the tests used in different centres, making the diagnostic process nonstandardised. There are limited data from other parts of the world, and a lack of antibody testing for autoimmune encephalitis in Africa, Asia and South America. Bedside assessment and clinical judgement remain critical in the diagnosis of encephalitis given that treatment is available, effective and often empirical based on presenting features (34, 35); however, this requires clinician awareness of the disease, which is often substandard in many areas.

IV aciclovir is widely available in high-income countries across Europe, North America and Australia but is often administered suboptimally and not in accordance with recommended guidelines (39, 40). Aciclovir availability appears to be variable in Asia, where it is mainly available in larger tertiary referral centres; however, there is within-country variation. Data for Africa and South America are sparse, but suggest that availability of IV aciclovir is limited and is even nonexistent in some countries. Where IV aciclovir is not available, oral valaciclovir may be preferable to oral aciclovir or nothing, because it has relatively good bioavailability and penetration into the CNS (41).

Disparities in prevention of encephalitis

Vaccines have had an enormous impact on global health, especially in LMIC. Vaccines are available for some causes of encephalitis, including JE virus, tick-borne encephalitis (TBE) virus, measles, rabies, dengue virus and VZV.

At present, about 70% of countries with a risk of JE virus transmission have immunization programmes in place. However, some countries have only introduced programmes in limited areas or have not achieved high coverage. The four main barriers to the introduction of a vaccine against JE by decision-makers in JE-endemic countries are lack of or limited disease surveillance, low financial resources, competing vaccine priorities and the need for technical assistance. It is not possible to eliminate JE virus from the environment because the virus is maintained in an enzootic cycle involving pigs, birds and mosquitoes. Therefore, high vaccination coverage must be maintained once programmes have been introduced, to avoid undoing the progress that has been made in controlling the disease (42).

Different immunization strategies for TBE exist, depending on the local epidemiological situation and the regional or national risk assessment. However, prevention of TBE is suboptimal, possibly due to underuse of vaccine in most countries with TBE, even in highly endemic areas. Climate change may alter the current distribution of TBE, and low endemic countries may see an increase in TBE burden (43).

The same risks could occur for other arthropod-borne viruses causing encephalitis, which are currently a focus of the WHO Global Arbovirus Initiative. The initiative is an integrated strategic plan to tackle emerging and re-emerging arboviruses with epidemic and pandemic potential. It focuses on monitoring risk, pandemic

prevention, preparedness, detection and response; and building a coalition of partners (44).

The average global coverage of two doses of measles-containing vaccine was 71% in 2021 – significantly lower than the 95% recommended by WHO (45). Many countries have yet to introduce a second dose as part of routine immunization and in 2018, more than 30% of children did not receive a second dose (46). As measles rates rise, a portion of children will continue to develop encephalitis concurrent with measles infection. Years later there will also be an increase in cases of subacute sclerosing panencephalitis, a fatal degenerative neurological condition (47). Vaccine hesitancy and limitations of health systems, including shortages of vaccine during certain periods of the year, contribute to gaps in vaccine coverage (46).

Pre-exposure rabies vaccination is recommended for individuals living in or travelling to countries or areas at risk, and in people at high risk of exposure to rabies, including laboratory staff working with rabies virus, veterinarians, animal handlers and wildlife officers. Prompt post-exposure prophylaxis (PEP) – including wound washing, administration of rabies vaccine and rabies immunoglobulin (RIG) where indicated – may be required following an animal bite or other contact with an animal suspected to be rabid in countries or areas at risk of rabies. In Africa, where access to the vaccine is limited, RIG is even less accessible than the vaccine (49). Vaccines can be administered by either the intradermal or intramuscular route for both pre-exposure prophylaxis and PEP; however, the intradermal route offers advantages because it uses 60–80% less vaccine volume; this lowers the vaccination cost, extends supplies and prevents shortages. Prompt provision of PEP remains a challenge in

rabies endemic areas owing to lack of a steady supply of PEP, delays in receiving PEP because of the long distances people have to travel to access health care, a lack of affordability of PEP, or poor health care seeking by people because of a lack of knowledge about the risk of rabies and its prevention (50). Efforts should focus on removing these barriers, to reach the WHO target of global elimination of dog-mediated rabies by 2030 (50). Despite its established efficacy, the varicella vaccine is not universally

part of routine immunizations, having only been recommended in 36 countries (51). Even so, 1 in 33 000–50 000 individuals who contract VZV will develop encephalitis (53). Barriers for VZV vaccination include the perception that VZV has a low risk of complications and the potential impact that vaccination programmes could have on the epidemiology of VZV infections, including the theoretical risk that it could lead to later onset and more severe varicella (chickenpox) and increased zoster incidence (54).

Lack of neurological workforce

Neurological disorders account for a large proportion of the global burden of disease, and the number of people living with neurological disorders is growing worldwide (55). Neurology health care professionals are needed to care for and manage this growing group; however, the available resources for neurological disorders globally are insufficient. The global median number of adult neurologists is 0.43 per 100 000 population, with a particular deficit of adult and child neurologists in LMIC (24). In the absence of neurologists, many people in LMIC consult primary care physicians or traditional healers, who lack training and expertise in neurological

disorders; therefore, early recognition of many neurological disorders is poor.

Data are sparse on the global distribution of other health care providers such as neuropsychologists, neuroradiologists and neurophysiologists. Moreover, neurorehabilitation services with specialist nurses and therapists are almost nonexistent (24). Considering the substantial burden of neurological sequelae in people who have survived encephalitis, the lack of interdisciplinary care and rehabilitation is of particular concern.

Responding to global encephalitis challenges: “Encephalitis as a public health priority” virtual stakeholder meeting

The global encephalitis policy context



The Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 aims to prioritize brain health and outlines five strategic objectives

The *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031* was adopted by the 75th World Health Assembly in May 2022 (57). The action plan aims to prioritize brain health and outlines five strategic objectives, relating to prioritization and governance; diagnosis, treatment and care; promotion and prevention; research, innovation and information systems; and a specific objective on the public health approach to epilepsy. Other WHO initiatives relevant to encephalitis include Defeating meningitis by 2030, a global roadmap (29), universal health coverage (58), the One Health approach to addressing zoonotic diseases (59), the Global vaccine action plan (60), the Vector control response 2017–30 (61), the Global framework for multi-disease elimination (62), the Global arbovirus initiative (44, 63) and programmes related to pathogen-specific WHO initiatives (e.g. JE, TBE, measles, rabies and VZV). The global burden of encephalitis will be reduced through harnessing these existing programs plus providing specific initiatives.

In February 2020, a preliminary report about encephalitis, accompanied by a petition signed by individuals from 128 countries, was presented to WHO by the Encephalitis Society and academic partners for World Encephalitis Day 2020. This was followed by a formal report titled *Encephalitis: an in-depth review and gap analysis of key variables affecting global disease burden* (56).

Building on these international efforts, participants came together during a 2-day virtual meeting entitled Encephalitis as a public health priority on 28–29 June 2022, to discuss global challenges posed by encephalitis and offer recommendations on which this report is based. Participants included representatives from 17 Member States including nongovernmental organizations (NGOs), academic institutions, WHO collaborating centres, technical experts, researchers, and people with encephalitis and their carers.

Consent to participate in the meeting was implied by participants accepting the

Emerging themes

Improving clinical and laboratory diagnosis of encephalitis

There is a clear need to improve the clinical and laboratory diagnosis of encephalitis globally. Suggestions on how health providers and systems can be strengthened to achieve this included training health care workers (including primary care physicians and other health care providers such as traditional healers) to ensure recognition and initial suspicion of encephalitis, raising awareness among the general public, tightening encephalitis case definitions and adapting them to local settings, and achieving early engagement of relevant stakeholders. Test availability is important to enable an accurate diagnosis of encephalitis, as is quality assurance and turnaround time. The need for a structured, tiered system of laboratory testing was highlighted, with local, national, subregional and regional diagnostic capabilities based around local epidemiology. Regional and subregional contacts were proposed to advise local staff (including nonspecialists) about the interpretation of laboratory results. There are WHO laboratory networks for some diseases

invitation from WHO and completing DOI and confidentiality forms. WHO technical staff collected and reviewed biographies and DOIs. Consultation with WHO's Quality Assurance Norms and Standards (QNS) methods support team and Compliance, Risk management and Ethics (CRE) unit was available if necessary. Experts were able to withdraw from the panel at any time.

A summary of the most salient points and themes across the panel sessions and discussions has been synthesized and is presented below, along with strategies for addressing the many challenges.

(e.g. measles and JE) that can provide technical support to countries and should be maintained or expanded; however, funding can be a challenge. Communication between clinicians and laboratory staff is essential to ensure that correct tests are performed and results fed back to ultimately have a positive influence on diagnosis and care.

Participants also discussed the clinical skills and knowledge needed by health care providers to make an accurate diagnosis of encephalitis. Clinicians in many LMIC have limited experience in diagnosing encephalitis and making the association between specific aetiologies and clinical presentations. Workforce training is needed to facilitate clinical diagnosis and interpretation of results, to minimize delays in diagnosis and subsequent treatment. Such training should cover the neurological workforce, primary care health workers, nurses, therapists and local traditional health practitioners, and it should be available in different languages to ensure global accessibility. Participants highlighted the need for LP skills as another important aspect, including how explain to people the importance of LPs, how to obtain consent, and training for clinicians in when LPs

are needed, what tests to order and where to transport the specimen.

Improving access to treatment and care for encephalitis

There are many challenges to equitable access to medicines and other treatments for encephalitis. Cost is a major issue, particularly in LMIC, where most expenses are out of pocket and national health care systems often do not adequately cover costs related to hospitalization, management and treatment. Further challenges include medication access in many LMIC. Aciclovir is generally available in tertiary care hospitals, but several participants commented that practices in rural areas have difficulty accessing the IV form of the drug. Medications for autoimmune encephalitis (e.g. IV immunoglobulin, rituximab and other immune therapies) are lacking in many regions globally. Incentives to companies to import these drugs and make them affordable for LMIC could be beneficial. Other challenges include insufficient hospitals in LMIC that can handle complex encephalitis cases, an unequal distribution of specialist clinicians in urban compared with rural areas, and insufficient medical workforces with expertise in encephalitis management and treatment.

Participants discussed ways to improve the recognition and management of neurological sequelae following encephalitis, which can have a devastating impact on families and society. For the recognition of sequelae, education of the neurological workforce, the health care workforce and the general public is essential. Participants emphasized the importance of a standard validated tool to minimize discrepancies in outcomes reported globally and to obtain accurate data on residual neurological sequelae.

For the management of sequelae, increased human resources are required to ensure an interdisciplinary approach. Supportive

management, including nursing and rehabilitation, is crucial in a low-income setting where treatment is unavailable. Simple, affordable strategies and approaches can be used to manage sequelae in resource-limited settings, and can substantially improve quality of life. Increased access to medicines used for the improvement of neurological sequelae is also important. There should be training in supportive therapies (e.g. pain management) for people with neurological sequelae, increased availability of medical devices (e.g. braces and orthotics) and training of surgeons in procedures such as selective dorsal rhizotomy. Centres of rehabilitation could be created based on strategic analyses (using population density and epidemiological disease data); these centres could also deliver medicines such as seizure and pain medication, as described for similar neurological deficits in the WHO Package of interventions for rehabilitation (64).

Lessons learned from the COVID-19 pandemic are also applicable to encephalitis; they include the importance of an interdisciplinary approach, early detection and the importance of vaccines.

Strategic approaches for preventing encephalitis

It was agreed that if vaccination programmes are to prevent encephalitis, advocacy (including accurate and tailored information) is essential along with integration into national programmes. Vaccination programmes and campaigns as described by WHO should be followed (65). Demonstrating where vaccination or other interventions have been particularly successful for encephalitis and resulted in reduced disease burden can be highly effective.

The role of vector control programmes in preventing encephalitis was discussed. Vector control should be considered as one strategic tool in a larger toolbox because work on vector control must consider climate change, urbanization, land uses and other anthropic

modification, water storage in urban and rural environments, and other environmental factors that affect vectors. The One Health concept recognizes that the health of humans, animals and the environment are linked and aims to address problems holistically by working across sectors to achieve the greatest impact (59). It was agreed that vector control should not come at the cost of vaccination. Using JE as an example, substantial effort is required to convince people that implementing mosquito control or vaccinating pigs was unlikely to have the same impact as human vaccination. The 2015 WHO JE vaccine position paper specifically states that “Adjunctive interventions, such as bed nets and mosquito control measures, should not divert efforts from childhood JE vaccination” (66).

More than 90% of human rabies infections are due to bites from rabid dogs. Vaccination of dogs can remove or reduce the risk of rabies transmission to humans. In many countries, dogs are culled as part of a strategy to eliminate rabies, but this only reduces rabies transmission temporarily – it does not solve the problem (67).

More needs to be done beyond vaccination and vector control for the prevention of encephalitis. Participants emphasized the importance of striving for the best available data to further understand the burden of disease and enable outbreak detection and rapid response. Furthermore, data regarding encephalitis outcomes are needed because such data can be used to advocate for and inform priorities in resource-limited settings. At the individual level, there is a need to understand what encephalitis is and what measures can be taken for personal protection.

Supporting people with encephalitis and their families

It is important that the voice of people living with the after-effects of encephalitis, and their carers, is incorporated into policies, plans, interventions and actions. Participants shared

their experiences of life after encephalitis or caring for individuals with encephalitis.

The primary issues for those affected by rabies, and their families, were discussed from experiences in India. Although rabies is preventable, even after exposure to the virus, some people never seek PEP owing to a lack of awareness. Even when they do seek treatment, health care workers must emphasize the necessity of completing the entire PEP treatment course to prevent serious consequences. Most hospitals in India refuse to admit people with rabies owing to lack of an effective cure and associated stigma; and, many die an agonizing death at home or in isolation hospitals. Increased awareness among health care providers and policy changes regarding admission to hospitals for supportive or palliative care are required. Family members of people with rabies often experience lack of closure given the rapid disease progression. In addition, affected families are often alone in their grief because deaths due to rabies are typically sporadic and isolated. Grief counselling services and support groups would be beneficial but are often lacking in LMIC.

Survivors and families play an important role in raising awareness of encephalitis and in supporting others who have been similarly affected by the condition. This is particularly important in countries where information regarding encephalitis is lacking. Social media platforms can be an a helpful tool; however, moderation by professionals knowledgeable about encephalitis is required to prevent misinformation. Harnessing the impact of regional, national and international community networks can be a useful source of support, particularly when third-sector partners (e.g. the Encephalitis Society) work with clinicians and academics to support these groups and networks, and ensure that the provided information is up to date and accurate.

Enhancing surveillance and research for encephalitis

Encephalitis surveillance is crucial for understanding the epidemiology, burden and distribution of disease; for guiding prevention measures and immunization campaigns; and for determining the efficacy of interventions, vaccine campaigns and vector control programmes. However, encephalitis surveillance presents numerous challenges. Encephalitis is a relatively uncommon condition that is often difficult to diagnose; hence, surveillance is largely syndromic. Syndromic surveillance case definitions cannot differentiate between infectious and autoimmune aetiologies of encephalitis. Different case definitions are used for encephalitis surveillance, complicating comparisons between settings. Laboratory-based surveillance, an important element of encephalitis surveillance, can be challenging in LMIC owing to unmet laboratory equipment needs, limited access or expensive diagnostic assays, difficulty with specimen handling, maintenance of the cold chain and specimen collection. Emerging pathogens present an ongoing challenge to encephalitis surveillance because they are often misdiagnosed, or diagnosis is delayed.

Participants agreed on the need for harmonized surveillance at the global level with defined aims; for example, whether to accurately diagnose every individual with encephalitis or to identify just enough cases to trigger action (e.g. JE vaccination). Participants agreed that the more complicated the surveillance, the less likely it will be pursued. Sentinel surveillance could be a way forward.

The potential need for surveillance of autoimmune encephalitis was discussed. This would require adequate diagnostics, which are lacking in many settings, even in some high-income countries. Participants agreed that diagnostics already included in the WHO EDL should be championed as a first priority. There is potential to consider what is missing from this list; however, implementation of the current list should come first.

The utility of databanks to pool information regarding encephalitis across countries was discussed. For autoimmune encephalitis, which is not yet fully understood, the way forward could be standard case definitions, standard approaches to surveillance and standard diagnostics, with subsequent pooling of data. Biobanks for infectious causes could be useful in parts of the world where diagnostics are less available, as a surveillance mechanism to revisit unappreciated outbreaks that may have occurred in the past and may inform empirical treatment regimens, possibly into the future when newer technologies can be used. Training with regards to the pragmatics of biobanking needs to focus on how to biobank samples, fund biobanks, ensure functionality of freezers and ensure samples are not degraded over time.

Some encephalitis research needs to include further understanding of autoimmune encephalitis, identification of biomarkers for encephalitis, better understanding of molecular mechanisms of disruption of the blood–brain barrier, understanding of neurotropism and understanding of the potential of immunomodulatory agents, in addition to antiviral medicines, to reduce sequelae from encephalitis.

Emerging themes



The main themes emerging from the meeting were the need for:

- information on the burden of encephalitis, including health economics data particularly in LMIC; better understanding of the severity of the disease (including disability and mortality); and strengthening routine health information systems;
- advocacy and awareness, including addressing stigma and discrimination and emphasizing the important role of people with encephalitis, their families and civil society organizations;
- improved diagnosis, public awareness and education materials for better diagnosis and care (including better support for rehabilitation);
- better treatment and care, including education and training of health care providers, integrated care across the continuum of services through universal health coverage, multidisciplinary care and improved access to affordable first-line medications;
- improved management of sequelae, including neurocognitive impairment, seizures and psychiatric symptoms;
- prevention, including advocacy for vaccines, integration of vaccines into national programmes, and vaccine education through primary care and community leaders;
- research and surveillance, including different types of surveillance, an encephalitis case definition that balances sensitivity and specificity, diagnostics with surveillance and globally harmonized surveillance (including sentinel surveillance sites with enhanced diagnostics); and
- support for people with encephalitis and their carers, including recognition of strategies to reduce carer burden including support, learning from other conditions and managing disinformation.

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Annex 1: List of participants

- **William Alford**, person with lived experience, United States of America (USA)
- **Philip Britton**, Associate Professor, Child and Adolescent Health, the Children's Hospital at Westmead, United Kingdom of Great Britain and Northern Ireland (United Kingdom)
- **Phillippa Chapman**, Deputy Chief Executive, Encephalitis Society, United Kingdom
- **Audrey Chishimba**, Neurologist, University Teaching Hospital, Zambia
- **Nicholas Davies**, Neurologist and Chair, Encephalitis Society Scientific Panel, United Kingdom
- **Anita Desai**, Professor, Diagnosis and Molecular Epidemiology of Viral Infections, National Institute of Mental Health and Neurosciences (NIMHANS), India
- **Ava Easton**, Chief Executive, Encephalitis Society, United Kingdom
- **Mark Ellul**, Neurologist and Vice-Chair, Encephalitis Society Board of Trustees, United Kingdom
- **David Garcia-Azorin**, Neurologist, Hospital Clínico Universitario de Valladolid, Spain
- **Matteo Gastaldi**, Neuroimmunologist, University of Pavia, Italy
- **Julia Granerod**, Epidemiologist, Dr JGW Consulting Ltd, United Kingdom
- **Jean-Michel Heraud**, Research Director, Institut Pasteur de Dakar, Senegal
- **Susan Hills**, Epidemiologist, Centers for Disease Control and Prevention (CDC), USA
- **Guan Hongzhi**, Professor, Chinese Academy of Medical Sciences and Peking Union Medical College, China
- **Cheryl Jones**, Head of School and Dean, University of Sydney School of Medicine; Professor of Paediatrics, Sydney Children's Hospital Network, Australia
- **Alain Kenfak**, Infectious Disease Consultant, Hôpital du Jura bernois, Switzerland
- **Frank Leypoldt**, Clinical Neuroimmunologist, University Hospital Schleswig-Holstein, Campus Kiel (UKSH) and Christian-Albrechts-University Kiel, Germany
- **Gareth Lipunga**, Research Fellow, Malawi-Liverpool-Wellcome Trust Programme, Malawi
- **Alejandra Mandujano**, person with encephalitis, Mexico
- **Reeta Mani**, Professor of Neurovirology, NIMHANS, India
- **Aline MB Matos**, Neurologist/Neuroimmunologist, Instituto de Medicina Tropical, Universidade de Sao Paulo, Brazil
- **Benedict Michael**, Senior Clinician Scientist Fellow, National Institute of Health and Social Care Research (NIHR) Health Protection Research Unit in Emerging and Zoonotic Infections and Honorary Consultant Neurologist, Walton Centre NHS Foundation Trust, United Kingdom

- **Mastura Monif**, Neurologist, Monash University Department of Neuroscience, Australia
- **Graham Niven**, family member of person with encephalitis
- **Ferron Ocampo**, Neurologist, International NeuroHIV Cure Consortium, Philippines
- **Ally Phillips**, Encephalitis Society, United Kingdom
- **Kameshwar Prasad**, Neurology consultant, Rajendra Institute of Medical Sciences, India
- **Ajit Rayamajhi**, Senior Paediatric Consultant, Kanti Children's Hospital, Nepal
- **Jim Sejvar**, Neuroepidemiologist, CDC, USA
- **Bhagteshwar Singh**, Clinical Research Fellow, Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, United Kingdom
- **Cristiane Soares**, Neurologist, Federal Hospital dos Servidores do Estado, Rio de Janeiro, Brazil
- **Tom Solomon**, Professor of Neurological Science; The Pandemic Institute, NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, Walton Centre NHS Foundation Trust and University of Liverpool, United Kingdom
- **Kiran Thakur**, Neurologist, Columbia University Irving Medical Center/New York Presbyterian Hospital, New York, USA
- **Arun Venkatesan**, Associate Professor, John Hopkins University School of Medicine; Director, Johns Hopkins Encephalitis Centre, USA
- **Tissa Wijeratne**, Chair, Department of Neurology, Western Health, Melbourne, Australia
- **Michael Wilson**, Associate Professor, Neurology, UCSF Weill Institute for Neuroscience, USA

WHO:

- **Bernadette Abela-Ridder**, Department of Neglected Tropical Diseases
- **Rodrigo Cataldi**, Brain Health Unit, Department of Mental Health and Substance Use
- **Tarun Dua**, Brain Health Unit, Department of Mental Health and Substance Use
- **Gergana Manolova**, Brain Health Unit, Department of Mental Health and Substance Use
- **Nicoline Schiess**, Brain Health Unit, Department of Mental Health and Substance Use
- **Heidi Soeters**, Immunization, Vaccines and Biologicals Department

Annex 2: Agenda

Encephalitis as a public health priority

Brain Health Unit | Department of Mental Health and Substance Use | World Health Organization
 Virtual meeting: 28 and 29 June 2022 | (13:00-16:00 Central European Time)

Time	DAY 1: Tuesday 28 June 2022	Speakers/Panellists
13:00 - 13:20	Welcome, Introduction & Objectives	Tarun Dua Nicoline Schiess Brain Health Unit WHO, Switzerland
13:20 - 13:35	Listening to people affected by encephalitis	Ava Easton, Encephalitis Society, United Kingdom
13:35 - 14:05	Encephalitis: Landscape Analysis	Julia Granerod Encephalitis Society, United Kingdom
14:05 - 14:25	Scope of the public health approach to encephalitis	Tom Solomon University of Liverpool, United Kingdom
14:25 - 14:40	Discussion	Discussant: Kameshwar Prasad, Rajendra Institute of Medical Sciences, India
14:40 - 14:50 Break		
14:50 - 15:25	Panel discussion: Part 1 Diagnosis Moderator: Mastura Monif, Van Cleef Centre for Nervous Diseases, Australia	Bhagteshwar Singh, University of Liverpool, United Kingdom, (India, Brazil) Anita Desai, National institute of mental health and neurosciences (NIMHANS), India Jean Michel Heraud, Institut Pasteur de Dakar, Senegal
15:25 - 16:00	Panel discussion: Part 2 Treatment and care Moderator: Kiran Thakur, Columbia University, New York, USA	Cristiane Soares, Federal Hospital dos Servidores do Estado, Brazil Ferron Ocampo, Bataan Doctors Hospital, Philippines. Ajit Rayamajhi, Kanti Children's Hospital, Nepal

Time	DAY 2: Wednesday 29 June 2022	Speakers/Panellists
13:00 - 13:10	Overview of preceding day	Benedict Michael, University of Liverpool, United Kingdom
13:10 - 13:50	Panel discussion: Part 3 Prevention (vaccines/vector control) Moderator: Susan Hills, CDC United States	Cheryl Jones, Sydney Children's Hospital Network, Australia Bernadette Abela-Ridder, WHO Department of Neglected Tropical Diseases, Switzerland Alain Kenfak, l'Hôpital du Jura Bernois, Switzerland
13:50 - 14:10	Presentation: Encephalitis surveillance/research	Jim Sejvar, Centers for Disease Control, USA
14:10 - 14:20	Discussion	
14:20 - 14:30 Break		
14:30 - 15:10	Panel discussion: Part 4 Supporting people with encephalitis and their families Moderator: Gareth Lipunga, Queen Elizabeth Central Hospital, Blantyre, Malawi	Reeta Mani, National institute of mental health and neurosciences (NIMHANS), India Matteo Gastaldi, University of Pavia, Italy María Alejandra Suárez – Person Affected by encephalitis, Mexico Graham Niven – Family Member. United Kingdom
15:10 - 15:45	Q&A	Nicoline Schiess, Brain Health Unit WHO, Switzerland
15:45 - 16:00	Meeting Summary and ways forward	Tarun Dua, Brain Health Unit WHO, Switzerland

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