

Current major event

Acute, severe hepatitis of unknown origin in children

On 5 April 2022, the International Health Regulations (2005) national focal point for the United Kingdom notified WHO of ten cases of severe acute hepatitis of unknown aetiology in previously healthy young children (across central Scotland). Since then, there have been continuing reports from multiple countries of cases of acute hepatitis of unknown origin among young children.

Editorial note

As of 21 April 2022, at least 169 cases of acute hepatitis of unknown origin have been reported from 11 countries in the WHO European Region and one country in the WHO Region of the Americas (see map). Cases have been reported in the United Kingdom of Great Britain and Northern Ireland (114), Spain (13), Israel (12), the United States of America (9), Denmark (6), Ireland (<5), the Netherlands (4), Italy (4), Norway (2), France (2), Romania (1) and Belgium (1). Cases are aged between one month to 16 years old. Seventeen children (approximately 10%) have required liver transplantation. At least one death has been reported.

The clinical syndrome among identified cases is acute hepatitis (liver inflammation) with markedly elevated liver enzymes. Many cases reported gastrointestinal symptoms including abdominal pain, diarrhoea and vomiting before presenting with severe acute hepatitis and increased levels of liver enzymes (aspartate transaminase (AST) or alanine aminotransaminase (ALT) greater the 500 IU/L) and jaundice. Most cases did not have a fever. The common viruses that cause acute viral hepatitis (hepatitis viruses A, B, C, D and E) have not been detected in any of these cases. International travel or links to other countries based on the currently available information have not been identified as factors.

Adenovirus has been detected in at least 74 cases, and of the number of cases with information on molecular testing, 18 have been identified as F type 41. SARS-CoV-2 was identified in 20 cases among those who were tested. Furthermore, 19 were detected with a SARS-CoV-2 and adenovirus co-infection.

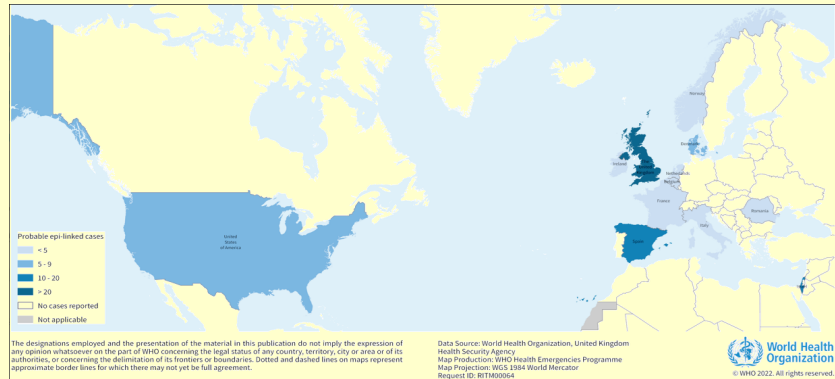
The United Kingdom, where the majority of cases have been reported to date, has recently observed a significant increase in adenovirus infections in the community (particularly detected in faecal samples from children) following low levels of circulation earlier in the COVID-19 pandemic. The Netherlands also reported a concurrent increase in community adenovirus circulation.

Nevertheless, due to enhancements in laboratory testing for adenovirus, this could represent the identification of an existing rare outcome that was occurring at levels not previously detected but is now being recognized due to increased testing.

Further investigations are ongoing in countries that have identified cases and include more detailed clinical and exposure histories, toxicology testing (i.e. environmental and food toxicity testing), and additional virological/microbiological tests. Affected countries have also initiated enhanced surveillance activities.

WHO and the European Centre for Disease Prevention and Control are supporting countries with the ongoing investigations and collecting information from the countries that are reporting cases. All available information is further disseminated by

Distribution of cases of acute severe hepatitis of unknown origin by country, as of 23 April 2022.



WHO's working case definition for acute severe hepatitis of unknown origin

Confirmed	Not available at present.
Probable	A person presenting with an acute hepatitis (non hepA–E*) with serum transaminase >500 IU/L (AST or ALT), who is 16 years and younger, since 1 October 2021.
Epi-linked	A person presenting with an acute hepatitis (non hepA–E*) of any age who is a close contact of a probable case, since 1 October 2021.
*If hepatitis A–E serology results are awaited, but other criteria met, these can be reported and will be classified as “pending classification”. Cases with other explanations for their clinical presentation are discarded.	

countries through their Hepatitis Networks and clinical organizations.

While adenovirus is currently one hypothesis as the underlying cause, it does not fully explain the severity of the clinical picture. Infection with adenovirus type 41, the implicated adenovirus type, has not previously been linked to such a clinical presentation.

Further work is required to identify additional cases, both in currently affected countries and elsewhere. The priority is to determine the cause of these cases to further refine control and prevention actions. Common prevention measures for adenovirus and other common infections involve regular hand washing and respiratory hygiene.

Member States are strongly encouraged to identify, investigate and report potential cases fitting the case definition. Epidemiological and risk factor information should be collected and submitted by Member States to WHO and partner agencies through agreed reporting mechanisms. Any epidemiological links between or among the cases might provide clues for tracking the source of illness. Temporal and geographical information about the cases, as well as their close contacts should be reviewed for potential risk factors.

WHO recommends that testing of blood, serum, urine, stool, and respiratory samples, as well as liver biopsy samples (when available) should be undertaken, with initial anecdotal experience showing whole blood to be more sensitive than serum. Further virus characterization can include sequencing. Other infectious and non-infectious causes need to be thoroughly investigated.

WHO does not recommend any restriction on travel and/or trade with the United Kingdom, or any other country where cases are identified, based on the currently available information.

Update on outbreaks in the Eastern Mediterranean Region

COVID-19 in 22 EMR countries

Current public health events of concern [cumulative N° of cases (deaths), CFR %]

Coronavirus disease 2019 (COVID-19): 2019–2022

Afghanistan	178 689	7682	4.3%
Bahrain	566 272	1475	0.26%
Djibouti	15 611	189	1.21%
Egypt	513 468	24 606	4.79%
Iran (Islamic Republic of)	7 216 040	140 975	1.95%
Iraq	2 324 223	25 205	1.08%
Jordan	1 695 745	14 064	0.83%
Kuwait	631 294	2555	0.40%
Lebanon	1 096 406	10 376	0.95%
Libya	501 904	6430	1.28%
Morocco	1 164 700	16 065	1.38%
occupied Palestinian territory	656 876	5657	0.86%
Oman	389 053	4257	1.09%
Pakistan	1 527 856	30 369	1.99%
Qatar	364 187	677	0.19%
Saudi Arabia	753 417	9078	1.20%
Somalia	26 485	1361	5.14%
Sudan	62 117	4931	7.94%
Syrian Arab Republic	55 797	3150	5.65%
Tunisia	1 039 532	28 533	2.74%
United Arab Emirates	897 136	2302	0.26%
Yemen	11 818	2149	18.18%