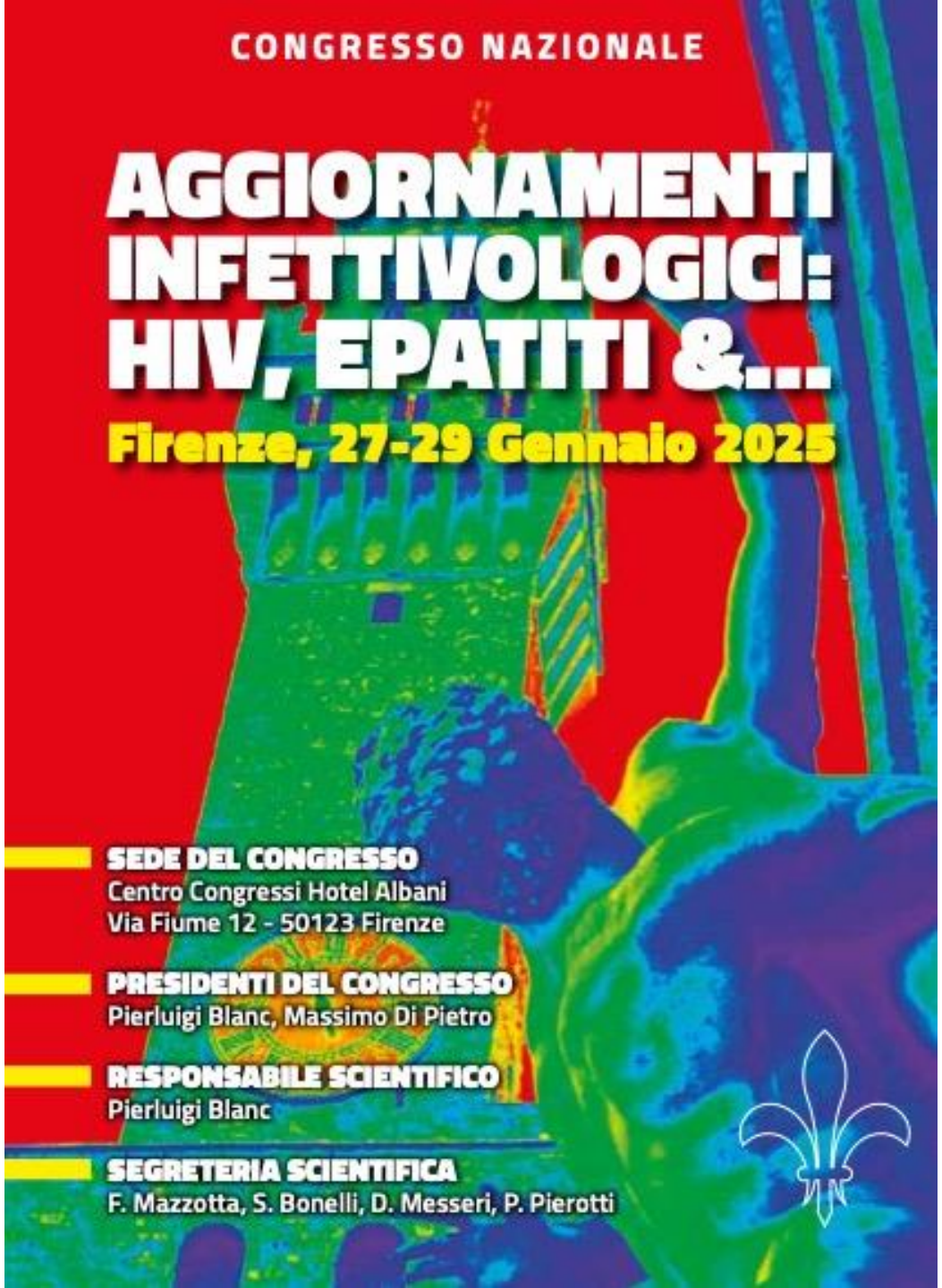


Le epatiti in pediatria: update

Giuseppe Indolfi

Department NEUROFARBA, University of Florence

Meyer Children's Hospital, IRCCS

Disclosures

Nothing to disclose

Agenda

Acute hepatitis

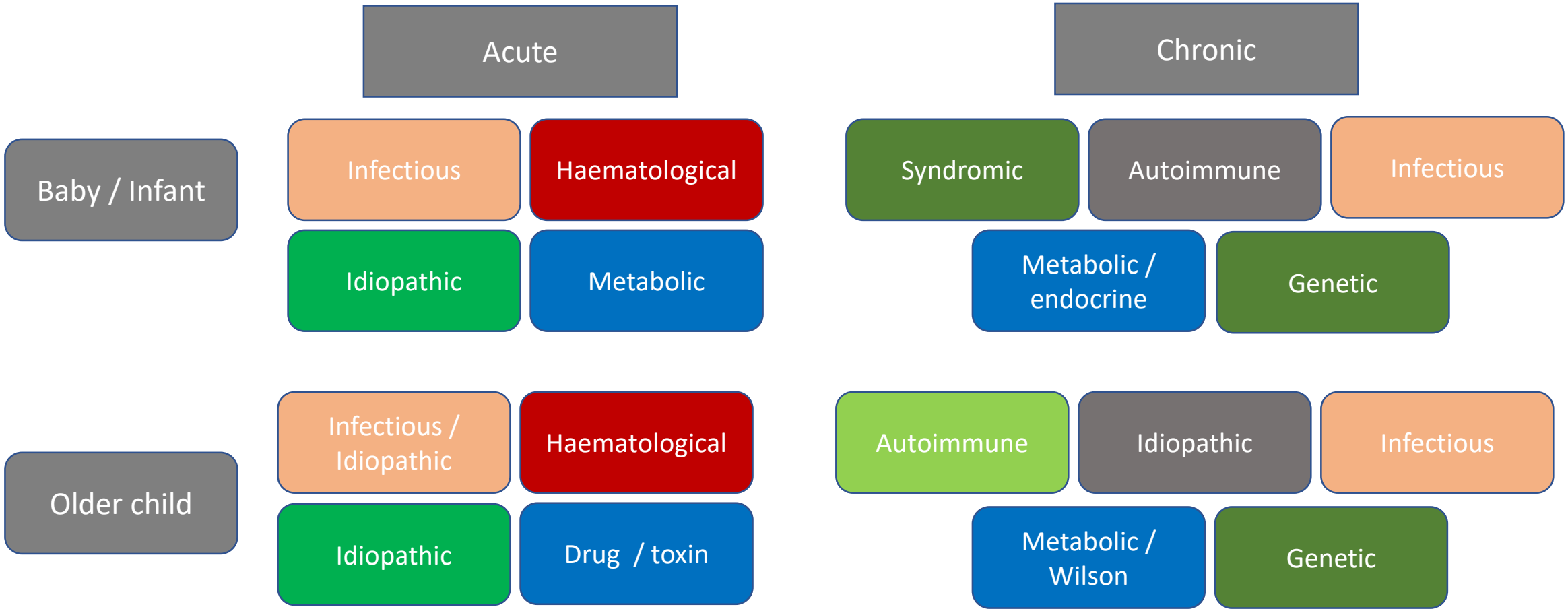
The Echovirus neonatal experience

Chronic hepatitis

Hepatitis C

Hepatitis B

Hepatitis in children: aetiology



Hepatitis in neonates

Infectious

Why neonates are immunologically different

Innate Immunity Reliance

Neonatal T cells are skewed towards innate immunity as compared with adult T cells

Limited Immunological Memory

Newborns have little immunological memory and a developing immune system

Distinct T Cell Populations

γδ T cells rapidly expand and functionally develop, serving as a primary defense against pathogens. In contrast, αβ T cells, which are more prevalent in adults, show limited development during this period.

Functional Differences in Immune Cells

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Severe and fatal neonatal infections linked to a new variant of echovirus 11, France, July 2022 to April 2023

Euro Surveill 2023 (June);28:2300253

Echovirus-11

- 9 severe neonatal infections
- 3–5 days-old
- all were male, eight were twins

- severe sepsis and liver failure
- fatal neonatal echovirus infections
  - 2022 - 2023: 8/496 (1.6%)
  - 2016 – 2021: 7/1,774(0.4%)

TABLE 1

Clinical characteristics of enterovirus-associated severe neonatal infections of male neonates with acute liver failure and multivisceral failure, France, 2022–2023 (n = 9)

Patient number	Gestation length (weeks+days)	Date of birth	Mode of delivery	Birth weight (g)	Age at first symptoms (days)	Specimen type	Age at diagnosis of EV infection (days)	Maternal EV infection	Maternal EV infection (days from delivery)	Treatment	Dialysis	Age at death (days)
1[a]	39+0	Jan 2023	Vaginal	3,480	5	CSF	5	Yes	0	Pocapavir D7-D21 IVIg D5	Yes	34
2	35+4	Dec 2022	Caesarian	2,400	5	Blood	5	Yes	-3[b]	IVIg D7, D8	Yes	19
3				2,650		Blood				IVIg D7, D8	Yes	40
4	31+5	Oct 2022	Vaginal	1,805	5	Blood	6	NA	NA	No	No	7
5				2,320		Post-mortem biopsies				No	No	6
6	36+3	Jul 2022	Vaginal	2,600	3	CSF	3	Yes	-3[b]	IVIg D4	No	5
7				2,860		CSF				IVIg D3, D4	No	5
8	34+0	Mar 2023	Vaginal	2,375	4	CSF	8	Yes	-1[b]	Pocapavir D8-D23 IVIg D18, 19	No	NA
9				1,970		CSF				Pocapavir D8-D23 IVIg D18, 19	No	NA

CSF: cerebrospinal fluid; IVIg: polyvalent intravenous immunoglobulins; NA: not applicable.

[a] From a singleton pregnancy.

[b] Days before delivery.

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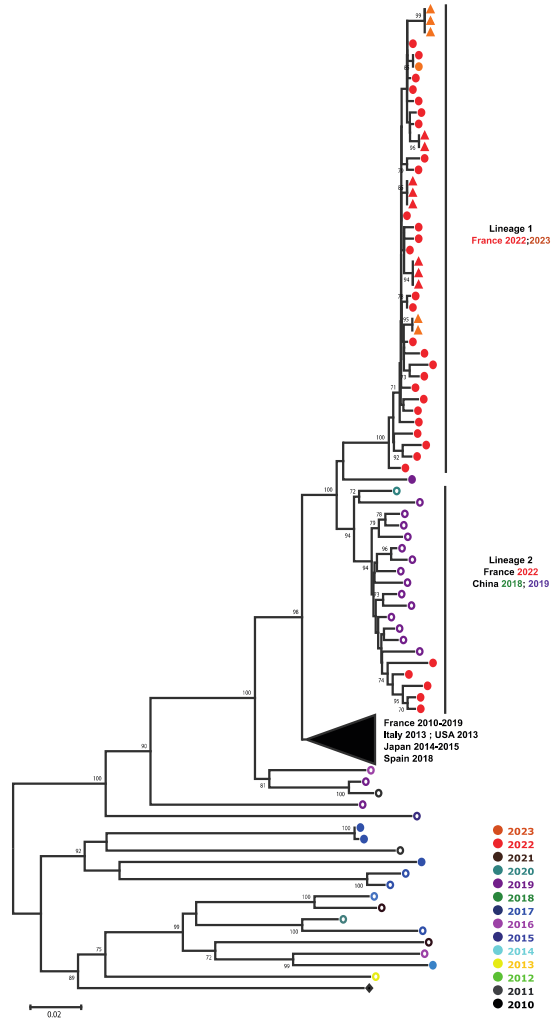
Severe and fatal neonatal infections linked to a new variant of echovirus 11, France, July 2022 to April 2023

Euro Surveill 2023;28:2300253

Echovirus-11

- Echovirus-11 detected in blood, cerebrospinal fluid, throat, nasopharyngeal or rectal swabs, stool, post-mortem biopsies or dried blood spots
- Maternal blood samples collected during the peripartum period were available for 4/5 mothers with gastrointestinal symptoms or fever during the 3 days before delivery
- All were Echovirus-11 positive



MEGA: molecular evolutionary genetics analysis.

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Mother to child transmission

Viruses

DNA Viruses

Hepatitis B Virus

Cytomegalovirus

Herpes Simplex Virus

Varicella-Zoster Virus

Human Parvovirus B19

RNA Viruses

HIV

Hepatitis C Virus

Zika Virus

Rubella Virus

Dengue Virus

SARS-CoV-2

Chikungunya Virus

Lassa Virus

HTLV1

Measles Virus

Ebola Virus

Fulminant echovirus 11 hepatitis in male non-identical twins in northern Italy, April 2023

Euro Surveill 2023 Jun;28:2300289

Echovirus-11

- Echovirus-11 in a pair of twins

- severe and fulminant hepatitis

Laboratory test	P1	P2	Reference range
Aspartate transaminase (mU/mL)	294	2,740	11.0–39.0
Alanine transaminase (mU/mL)	291	11,925	11.0–34.0
Gamma-GT (mU/mL)	191	202	11.0–53.0
Creatinine (mg/dL)	0.39	0.46	0.30–0.70
Total bilirubin (mg/dL)	2.11	11.28	0.2–1.1
Direct bilirubin (mg/dL)	Not available	2.73	0.00–0.25
Plasma prothrombin (%)	94.00	Undetectable	70.00–120.00
Thromboplastin time (s)	42.90	Undetectable	20.00–32.00
Fibrinogen (mg/dL)	374	Undetectable	170–410
International normalised ratio	1.03	Unmeasurable	0.90–1.20
Hepatic cholinesterase (mU/mL)	5,656	2,986	5,300–12,900
Plasma ammonium (µg/dL)	160	192	19.0–94.0
Ferritin (ng/mL)	2,542	124,801	8–398

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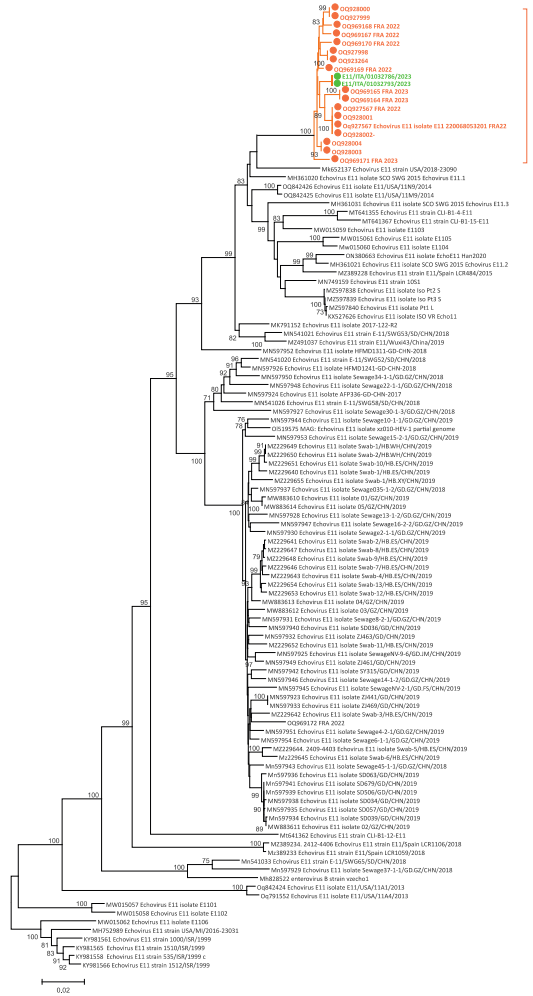
Fulminant echovirus 11 hepatitis in male non-identical twins in northern Italy, April 2023

Euro Surveill 2023 Jun;28:2300289

Echovirus-11

- The Echovirus-11 genome showed 99% nucleotide identity with E11 strains reported in the cases in France

- green: sequences from the two neonates reported Italy
- orange: sequences from neonatal cases reported in France



Green: sequences from the two neonates reported in this manuscript; orange: sequences from neonatal cases reported in France [2].

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Disease Outbreak News

Enterovirus-Echovirus 11 Infection - the European Region

7 July 2023

Situation at a glance

Since the Disease Outbreak News published on 31 May 2023 which reported enterovirus, Echovirus 11 (E-11) infection in France, additional Member States in the European Region have notified WHO of cases of E-11 among newborns. As of 26 June 2023, Croatia, Italy, Spain, Sweden, and the United Kingdom of Great Britain and Northern Ireland have reported cases of E-11 infection confirmed in newborns. Further investigations and public health responses are being implemented in each of these Member States. This Disease Outbreak News provides updates on the event and the public health response implemented in the reporting and non-reporting countries in the European Region. Based on the limited information available, WHO assesses the public health risk for the general population to be low, while we continue to encourage countries to monitor for and report on cases. Health facilities caring for newborns should familiarize themselves with the signs and symptoms of echovirus and maintain vigilance for potential healthcare-associated infections and outbreaks.

Description of the situation

On 5 May 2023, France reported an increase in cases of severe neonatal sepsis associated with Enterovirus (Echovirus-11 (E-11)). A total of nine cases of neonatal sepsis with hepatic impairment and multi-organ failure with seven deaths were reported between July 2022 and April 2023 from four hospitals in three regions of France.

As of 26 June 2023, Croatia reported one confirmed case of E-11 infection from a cluster of enterovirus diseases in neonates detected in June 2023, Italy has reported seven cases of E-11 infection confirmed in neonates between April and June 2023, Spain reported two cases of E-11 infection in 2023, Sweden reported five E-11 cases with four cases of meningoencephalitis among infants due to E-11 infection between 2022 and 15 June 2023, and the United Kingdom of Great Britain and Northern Ireland (the UK) reported two cases in March 2023.

See all DONs related to this event

Read more about

Neonatal acute liver failure cases with echovirus 11 infections, Japan, August to November 2024

Euro Surveill 2025 (Jan);30:2400822

Echovirus-11

- August–November 2024
- 3 neonatal cases of acute liver failure with echovirus 11 in Tokyo
- all neonates developed irreversible multiple-organ failure and died

Characteristics	Case 1	Case 2	Case 3
Clinical background			
Month of onset in 2024	August	August	November
Age at onset (days)	7	8	8
Gestational age (weeks + days)	38 + 3	37 + 0	37 + 4
Birth weight (g)	2,674	2,454	2,300
Sex	Male	Male	Male
Delivery	Normal vaginal delivery	Caesarean section	Caesarean section
Sick contacts	Father (fever)	None	None
Diagnosis	ALF, HLH, Torsades de pointes, renal failure	ALF, HLH, renal failure	ALF, renal failure
Known underlying diseases	None	None	None
Outcome	Died	Died	Died
Laboratory results			
Serum PCR[a]	EV	EV	EV
EV genotype (GenBank accession number)	Echovirus 11 (LC849101)	Echovirus 11 (LC855180)	Echovirus 11 (LC855181)
FilmArray respiratory panel[b]	Not performed	HRV/EV	HRV/EV

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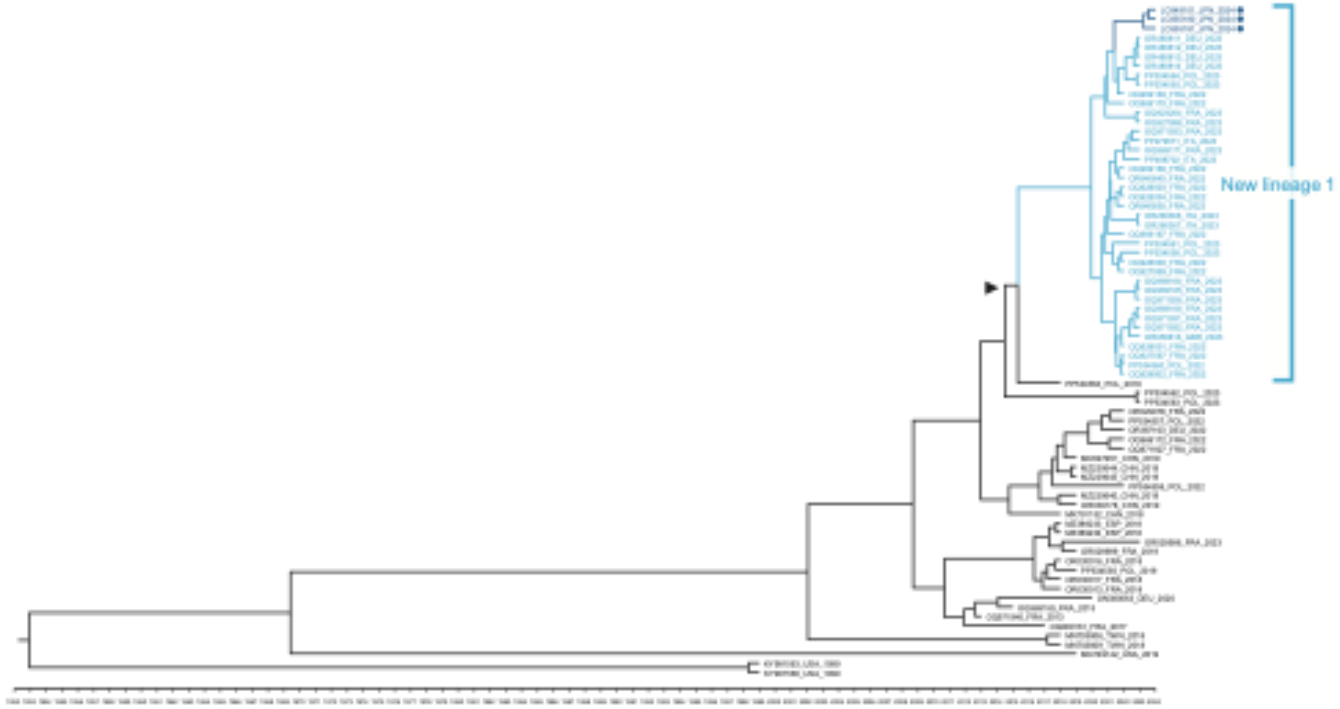
Neonatal acute liver failure cases with echovirus 11 infections, Japan, August to November 2024

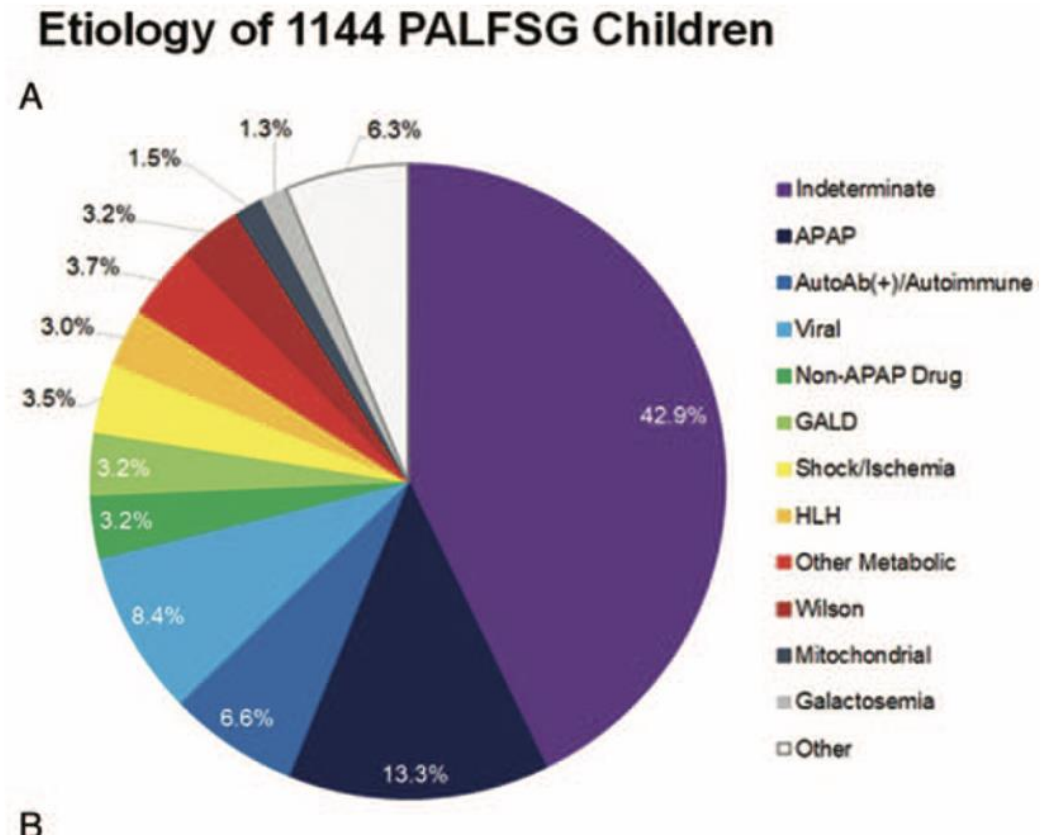
Euro Surveill 2025 (Jan);30:2400822

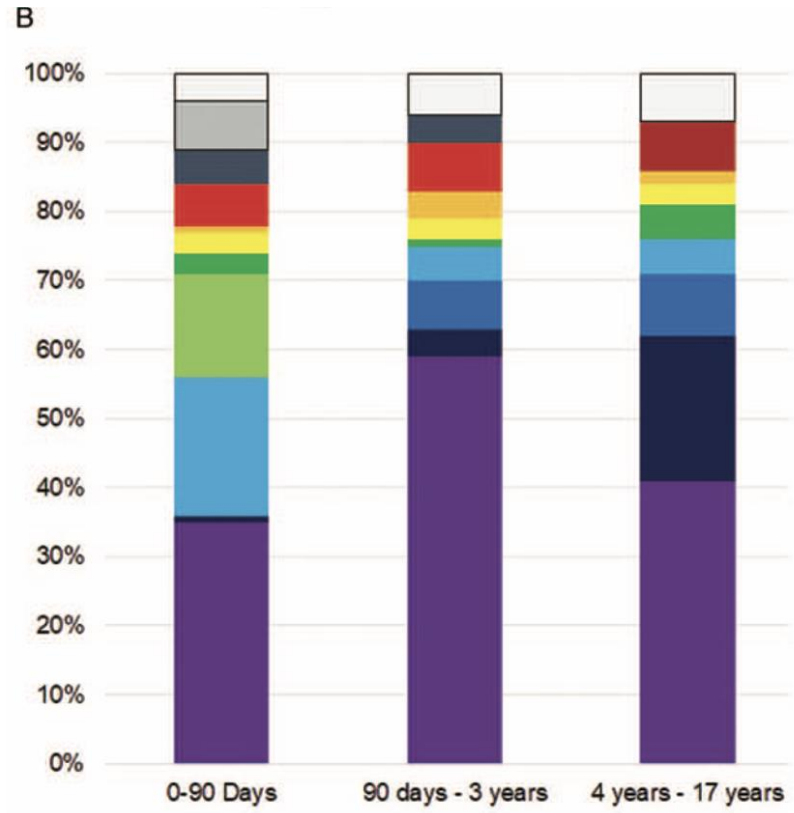
Echovirus-11

- The Echovirus-11 strain belonged to the new lineage 1, which was the same as strains isolated from neonatal ALF cases in Europe in 2022–23



PALF-SG: aetiology of ALF





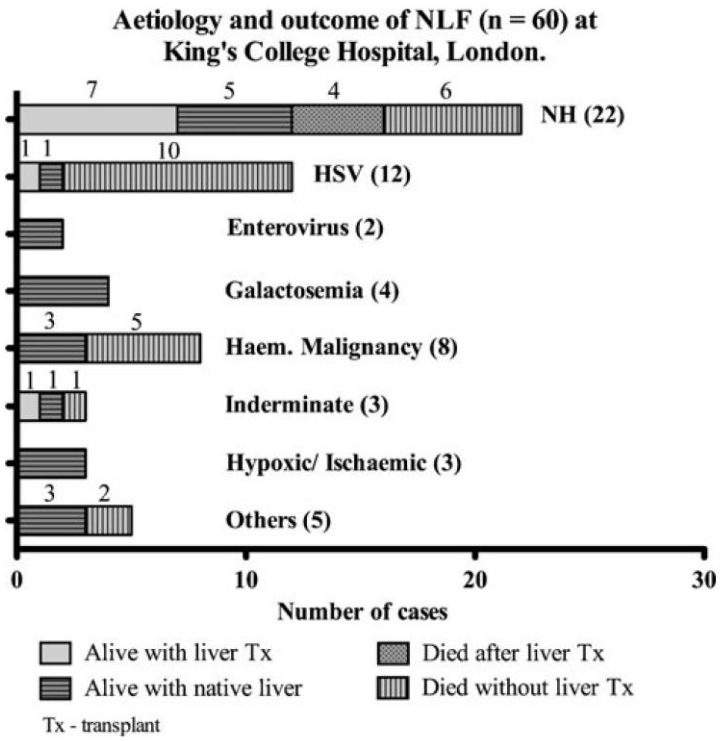
Survived native liver 54%, Transplant 30%

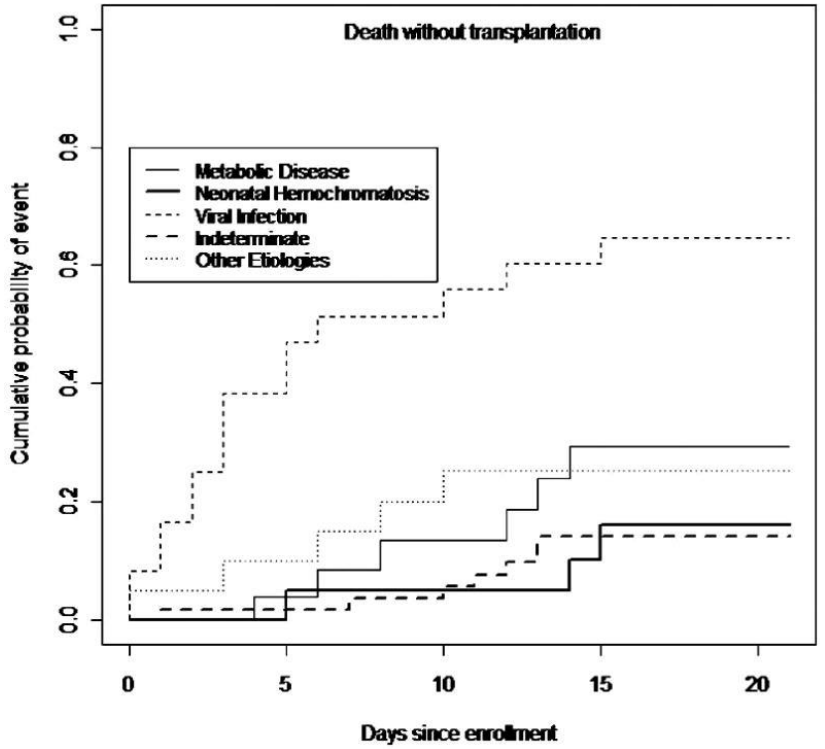
Model: dynamic INR, Bilirubin, encephalopathy

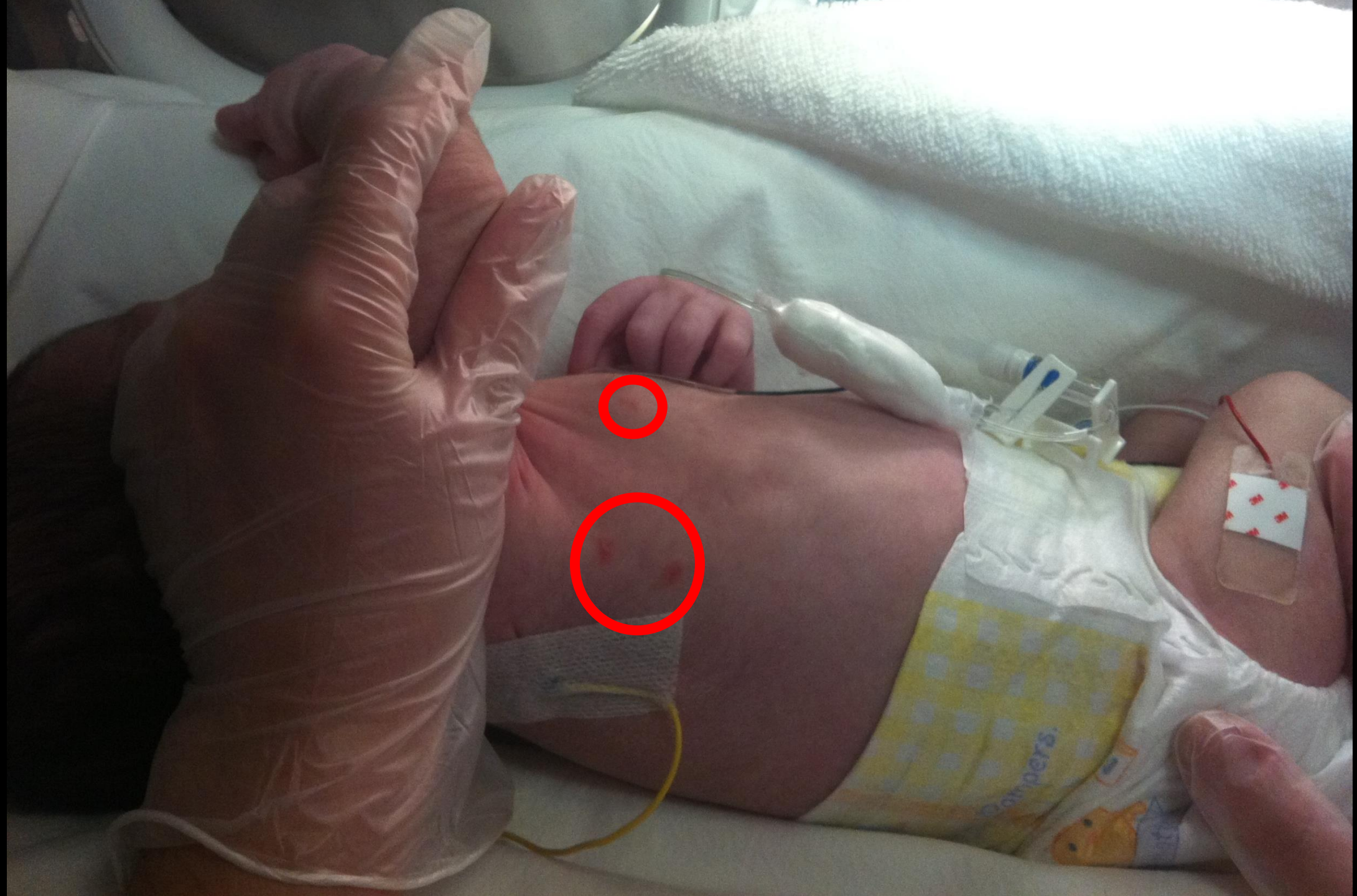
Squires et al. for NASPGHAN, JPGN 2022

Neonatal liver failure: aetiologies and management—state of the art

Eur J Pediatr 2011;170:573–581






Pampers

ORIGINAL ARTICLE

A Case Series of Children with Acute Hepatitis and Human Adenovirus Infection

L. Helena Gutierrez Sanchez, M.D., Henry Shiau, M.D., Julia M. Baker, Ph.D., Stephanie Saaybi, M.D., Markus Buchfellner, M.D., William Britt, M.D., Veronica Sanchez, Ph.D., Jennifer L. Potter, M.P.H., L. Amanda Ingram, M.P.H., David Kelly, M.D., Xiaoyan Lu, M.S., Stephanie Ayers-Millsap, M.P.H., Wesley G. Willeford, M.D., Negar Rassaei, M.D., Julu Bhatnagar, Ph.D., Hannah Bullock, Ph.D., Sarah Reagan-Steiner, M.D., Ali Martin, B.S., Michael E. Rogers, D.O., M.P.H., Anna M. Banc-Husu, M.D., Sanjiv Harpavat, M.D., Ph.D., Daniel H. Leung, M.D., Elizabeth A. Moulton, M.D., Ph.D., Daryl M. Lamson, B.S., Kirsten St. George, Ph.D., Aron J. Hall, D.V.M., Umesh Parashar, M.D., Adam MacNeil, Ph.D., Jacqueline E. Tate, Ph.D., and Hannah L. Kirking, M.D.

ORIGINAL ARTICLE

Clinical Spectrum of Children with Acute Hepatitis of Unknown Cause

Chayarani Kelgeri, M.D., Michael Couper, M.B., Ch.B., Girish L. Gupte, M.D., Alexandra Brant, M.Sc., Mitul Patel, M.D., Lauren Johansen, M.B., B.S., Joseph Valamparampil, M.D., Evelyn Ong, F.R.C.S., Hermien Hartog, Ph.D., M.T.P.R. Perera, M.D., Darius Mirza, M.S., F.R.C.S., Indra van Mourik, M.D., Khalid Sharif, F.R.C.S., F.C.P.S., and Jane Hartley, M.Med.Sc., Ph.D.

Article

Adeno-associated virus 2 infection in children with non-A–E hepatitis

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Check for updates

Antonia Ho[1,206], Richard Orton[1,206], Rachel Tayler[2,206], Patawee Asamaphan[1,206], Vanessa Herder[1,206], Chris Davis[1,206], Lily Tong[1], Katherine Smollett[1], Maria Manali[1], Jay Allan[1], Konrad Rawlik[3], Sarah E. McDonald[1], Elen Vink[1], Louisa Pollock[1,2], Louise Gannon[4], Clair Evans[5], Jim McMenamin[6], Kirsty Roy[6], Kimberly Marsh[6], Titus Divala[6], Matthew T. G. Holden[6], Michael Lockhart[6], David Yirrell[6], Sandra Currie[6], Maureen O'Leary[6], David Henderson[6], Samantha J. Shepherd[7], Celia Jackson[7], Rory Gunson[7], Alasdair MacLean[7], Neil McInnes[7], Amanda Bradley-Stewart[8], Richard Battle[8], Jill A. Hollenbach[10], Paul Henderson[11], Miranda Odam[12], Primrose Chikowore[13], Wilna Oosthuyzen[13], Meera Chand[12], Melissa Shea Hamilton[13], Diego Estrada-Rivadeneyra[13], Michael Levin[13], Nikos Avramidis[3], Erola Pairo-Castineira[3], Veronique Vitart[3,14], Craig Wilkie[15], DIAMONDS Consortium*, ISARIC4C Investigators, Massimo Palmarini[1], Surajit Ray[16], David L. Robertson[1,207], Ana da Silva Filipe[1,207], Brian J. Willett[1,207], Judith Breuer[16,207], Malcolm G. Semple[17,207], David Turner[9,207], J. Kenneth Baillie[2,14,207] & Emma C. Thomson[1,16,207]✉

Article

Genomic investigations of unexplained acute hepatitis in children

Article

Adeno-associated virus type 2 in US children with acute severe hepatitis

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Check for updates

Venice Servellita[1,22], Alicia Sotomayor Gonzalez[1,22], Daryl M. Lamson[2,22], Abiodun Foresythe[1], Hee Jae Huh[1,3], Adam L. Bazinet[4], Nicholas H. Bergman[4], Robert L. Bull[5], Karla Y. Garcia[4], Jennifer S. Goodrich[4], Sean P. Lovett[4], Kisha Parker[4], Diana Radune[4], April Hatada[6], Chao-Yang Pan[6], Kyle Rizzo[6], J. Bradford Bertumen[6,7], Christina Morales[6], Paul E. Olunyi[6], Jenny Nguyen[1], Jessica Tan[1], Doug Stryke[1], Rayah Jaber[8], Matthew T. Leslie[9], Zin Lyons[10], Hayden D. Hedman[2,11], Umesh Parashar[12], Maureen Sullivan[12], Kelly Wrobleski[12], M. Steven Oberste[7], Jacqueline E. Tate[7], Julia M. Baker[7], David Sugerman[7], Caelin Potts[7], Xiaoyan Lu[7], Preeti Chhabra[7], Pediatric Hepatitis of Unknown Etiology Working Group*, L. Amanda Ingram[13], Henry Shiau[14], William Britt[14], Luz Helena Gutierrez Sanchez[14], Caroline Ciric[15], Christina A. Rostad[15], Jan Vinjé[7], Hannah L. Kirking[7], Debra A. Wadford[6], R. Taylor Raborn[4], Kirsten St. George[2,16] & Charles Y. Chiu[1,17,18]✉

nature

https://doi.org/10.1038/d41586-023-00570-8

News & views

Medical research

Childhood hepatitis outbreak under scrutiny

Frank Tacke

Since 2022, more than 1,000 cases of childhood hepatitis with no known cause have been reported. The discovery of adeno-associated virus 2 in the blood and livers of such children might provide an explanation.

Paediatricians first began to report a concerning wave of acute severe hepatitis — a disease involving liver inflammation — in children in spring 2022. This spate of cases, which now numbers more than 1,000 (see go.nature.com/42dpfv4), had no known cause, unlike most cases of paediatric hepatitis. The cases were often serious, with 7.3% of affected children needing a liver transplant[1]. Writing in *Nature*, three groups now independently provide evidence that infection by adeno-associated virus 2 (AAV2) is linked to this wave[2–4]. Their work is likely to spark debate, and could influence disease management.

Two previous analyses[5,6] of this wave of acute severe hepatitis found an association with human adenovirus (HAdV), particularly the HAdV-F41 strain. However, this result has puzzled clinicians because, although adenovirus-induced hepatitis is a known phenomenon, it is rare and usually restricted to people with severely compromised immune systems. Moreover, the studies identified various HAdV strains, even in children from the same geographical region, implying that a single strain could not explain these hepatitis outbreaks. Furthermore, adenovirus-induced hepatitis is characterized by virus-derived structures, called inclusions, in the nucleus — something that has not often been detected in the current outbreak[7].

Controversy therefore remained around whether the outbreak was caused by HAdV or another virus. The previous studies identified HAdV using targeted genetic-sequencing approaches. By contrast, the current studies involved an untargeted approach called clinical metagenomics, in which all nucleic acids from a sample are sequenced, to discover which viruses might be present. All three identified AAV2 — a virus known to replicate in the liver, but not known to cause hepatitis[8].

In the first of the papers, Ho *et al.*[2] report high levels of AAV2 in blood and liver samples from 26 (81%) out of 32 affected children in the United Kingdom. By contrast, the researchers detected only low AAV2 levels in 5 (7%) of 74 members of a control group consisting of healthy children, children who had HAdV infection but not hepatitis, or children who had other diseases or other forms of acute hepatitis. The authors found that 93% of the affected group carried a gene variant that predisposes an individual to autoimmune diseases involving immune cells called T cells. Liver biopsies were available for five infected children. Analysis using a tissue-staining approach (histology) revealed AAV2 in abnormally swollen liver cells (hepatocytes) surrounded by T cells, suggesting a causative role of AAV2 in acute hepatitis.

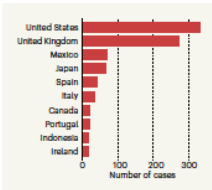

Figure 1 | Hepatitis outbreak around the world. As of July 2022, 35 countries had reported cases of severe acute paediatric hepatitis that had no known cause, according to the World Health Organization (see go.nature.com/42dpfv4). Numbers for the 10 countries with most reported cases are shown here. Three groups[2–4] now provide evidence that adeno-associated virus 2 has a role in this outbreak.

In the second study, also from the United Kingdom, Morfopoulou *et al.*[3] report high levels of AAV2 in 27 of 28 affected children, and only low levels of AAV2 in a control group, which included immunocompromised children who had acute hepatitis due to other causes, and children with normal immune systems who had fever. The authors used several techniques to demonstrate that the disease was not due to direct damage to hepatocytes (known as hepatotoxicity) caused by AAV2 alone. Because low levels of HAdV and human herpesvirus 6B (HHV-6B) were detected in the liver in most cases, the authors speculate that these viruses might enable AAV2 replication, leading to damage to hepatocytes.

In the third paper, Servellita *et al.*[4] report similar findings from the United States. They detect AAV2 in 13 of 14 cases, compared with only 4 of 113 controls. All 14 cases also tested positive for HAdV. In the 13 children infected with AAV2, the authors found co-infection with a 'helper' virus that might promote AAV2 replication — either Epstein–Barr virus (EBV) or HHV-6. Thus, most of the cases had a triple infection (AAV2, HAdV and either EBV or HHV-6). The fact that these authors examined only children who were infected with HAdV might explain why they detected more concomitant viral infections than did the other groups.

All three studies make the same observation of AAV2 in children with unexplained acute hepatitis. That the studies took place on two continents adds to their value, given the global nature of the outbreak (Fig. 1). However, a note of caution is needed — these studies were all conducted retrospectively, rather than being gold-standard prospective trials, in which subjects are selected for study, with data being subsequently collected over time. The case numbers are relatively small, and the number of liver samples even smaller. The studies report limited clinical information (such as ethnic background, whether the children were born by caesarean section and whether they could have been exposed to viruses during day care), which is needed to reveal potential factors or co-factors in disease development. Such data would be essential to exclude the possibility that AAV2 is a harmless bystander.

Direct evidence for how AAV2 might cause hepatitis is limited. Ho and co-workers' genetic and histological analyses imply that the disease is rooted in abnormal immune responses, rather than in a hepatotoxic role for AAV2. Morfopoulou and colleagues provide support

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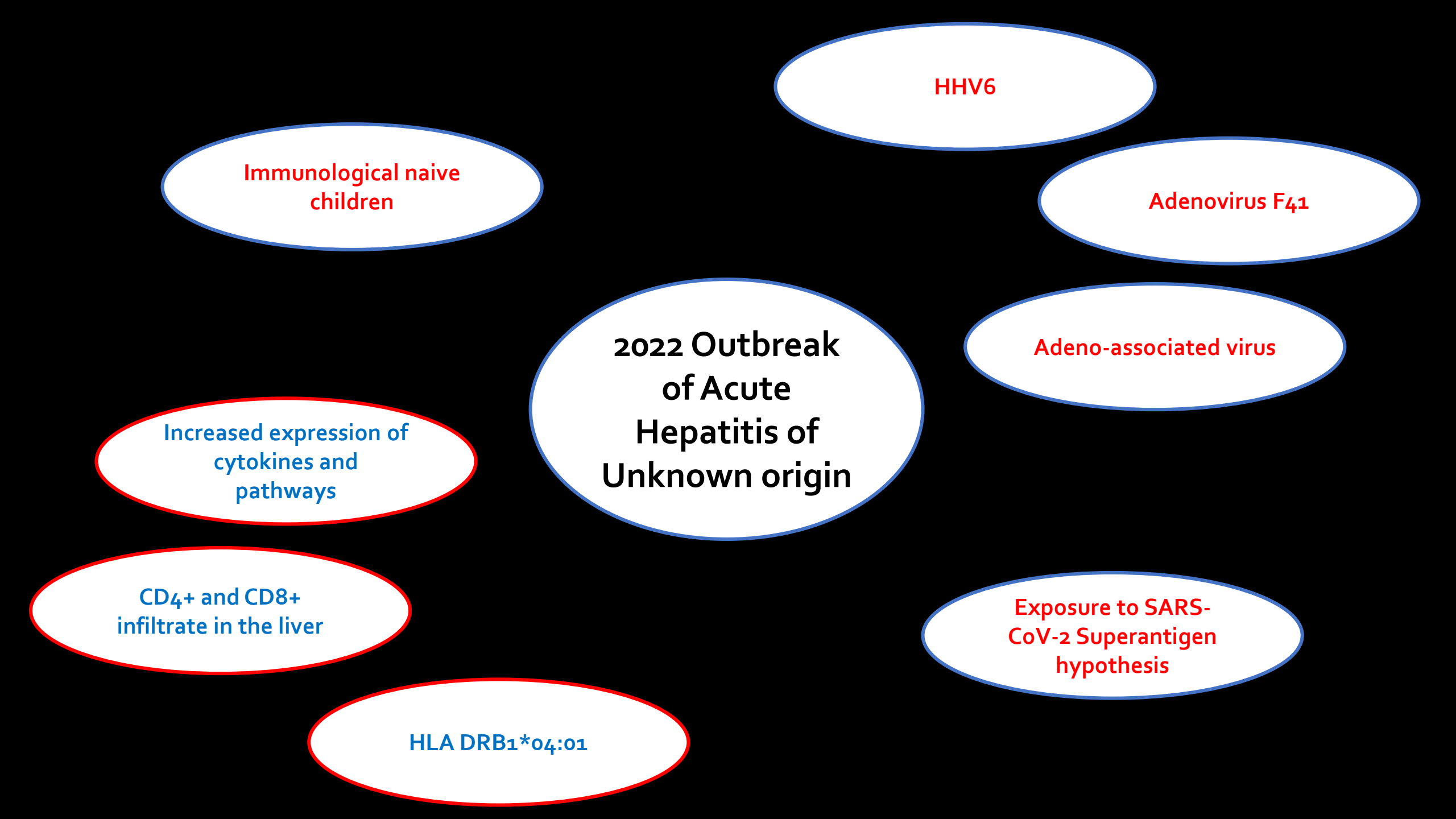
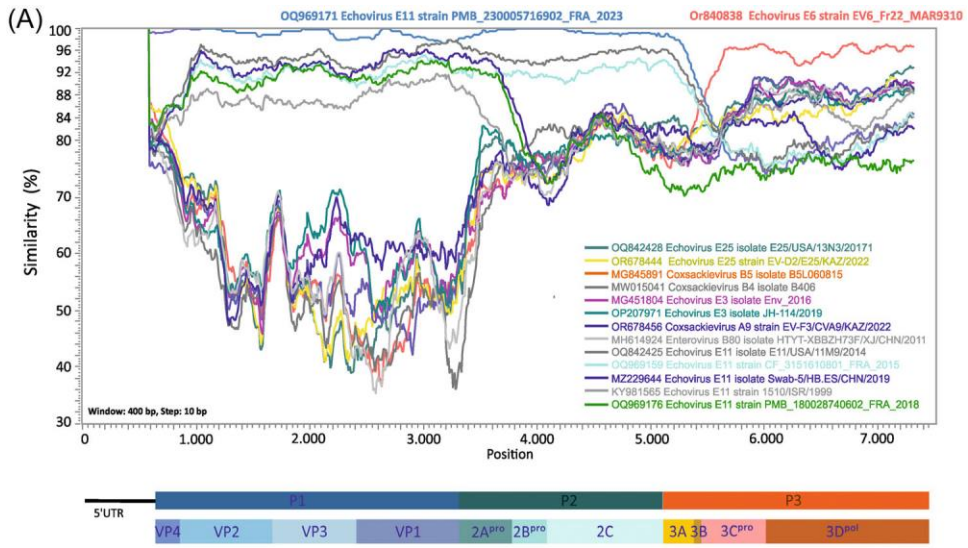

HHV6
Immunological naive children
Adenovirus F41
2022 Outbreak of Acute Hepatitis of Unknown origin
Adeno-associated virus
Increased expression of cytokines and pathways
CD4+ and CD8+ infiltrate in the liver
Exposure to SARS-CoV-2 Superantigen hypothesis
HLA DRB1*04:01

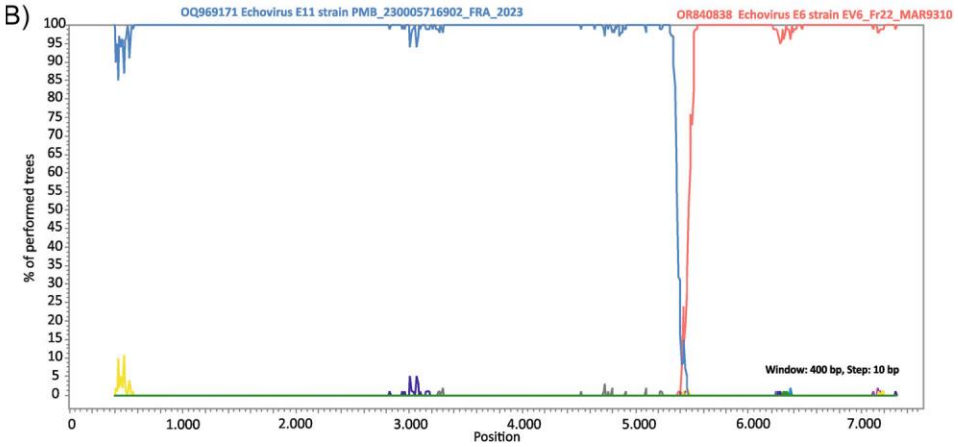
Molecular characterization of emerging Echovirus 11 (E11) shed light on the recombinant origin of a variant associated with severe hepatitis in neonates

J Med Virol 2024;96:e29658

- Italian strains belonged to genogroup D5, similarly to other E11 strains recently reported in France and Germany all together aggregated into separate clusters

- Echovirus 6 was identified as the major recombinant virus in 3Cpro and 3Dpol regions





Christian, 4 years old

24 August 2024
Pediatria Medica A, Meyer IRCCS

- Fever for 2 days

Day 2

  - AST 140 IU/L
  - ALT 193 IU/L

- Fever

Day 6

  - ALT 7000 IU/L
  - INR 2.6
  - direct bilirubin 3.9 mg/dL

Meyer (8 hours)

  - ALT 14.000 IU/L
  - INR 3.6

Liver transplant centre

  - encephalopathy
  - INR 5

Supportive treatment

Plasmapheresis

Echovirus positive blood, CSF, throat

Unpublished case

Meyer

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Enterovirus

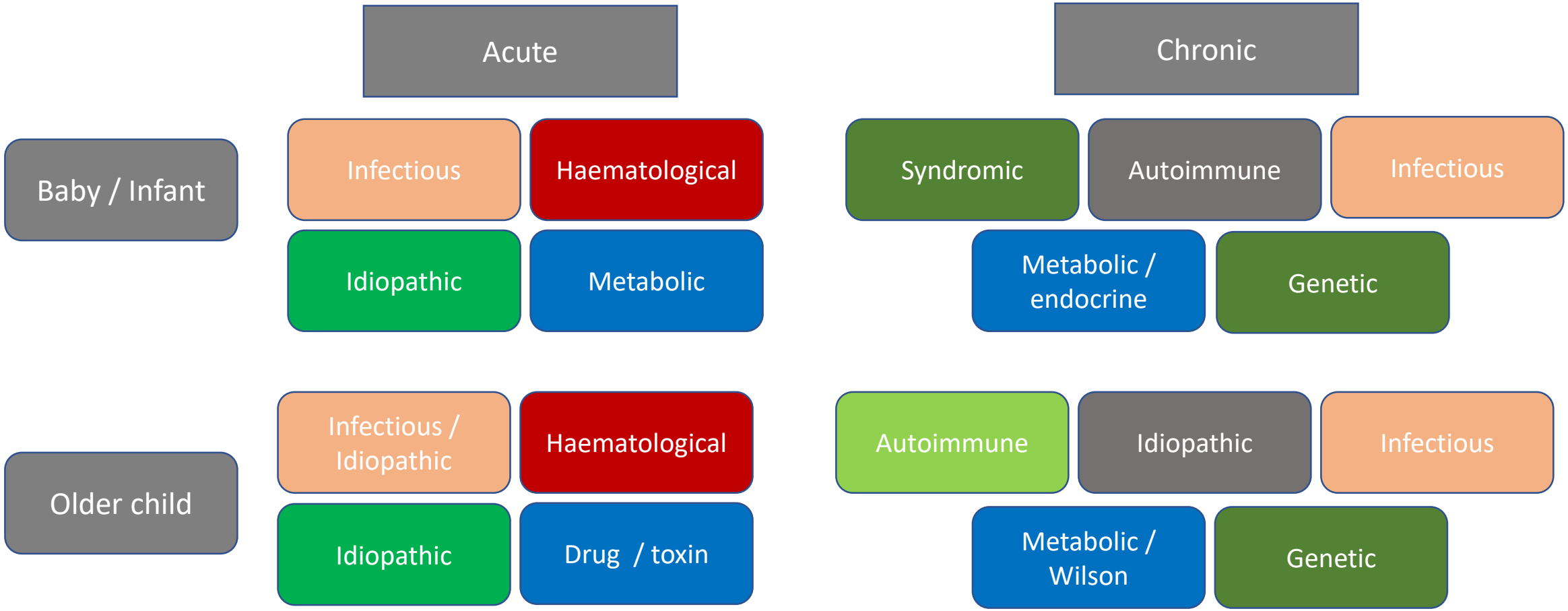
Infectious

Therapeutic options

- Supportive care
- Intravenous immunoglobulin
- Experimental antiviral agents
  - pleconaril (in vitro activity, not available commercially)
  - Pocapavir (treatment of chronic poliovirus infection in immunodeficient patients, not commercially, compassionate use)
- Preventive measures

American Academy of Pediatrics. Book: 2024 Report of the Committee on Infectious Diseases. 2024

Hepatitis in children: aetiology



Hepatitis in children: chronic infections

Infectious

WHO updated guidelines

Treat all adults and adolescents (aged ≥12 years) with chronic hepatitis AND:

- Evidence of fibrosis (≥ F2) or cirrhosis (F4) based on
  - clinical criteria or
  - APRI score of ≥ 0.5 or
  - transient elastography value of ≥8.3 Kpa*, regardless of HBV DNA or ALT levels

- **HBV DNA >2000 IU/ml** and an **ALT level above ULN** (30 U/L for men and 19 U/L for women)

- Presence of co-infections, family history of liver cancer or cirrhosis, co-morbidities

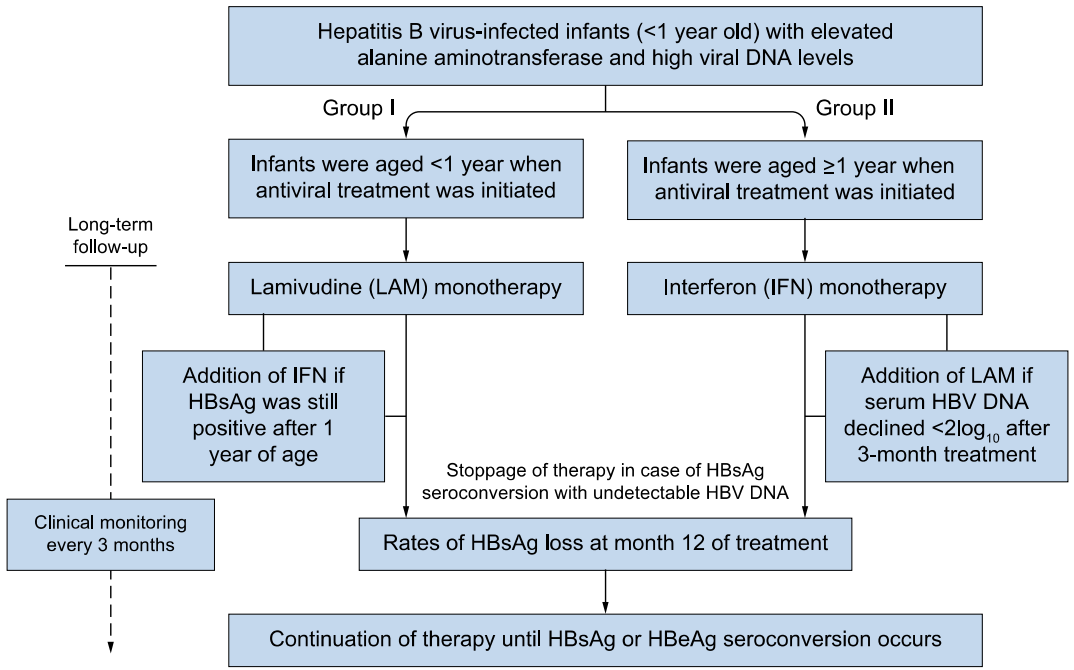
- Persistently abnormal ALT levels (in absence of access to an HBV DNA assay), regardless of APRI score

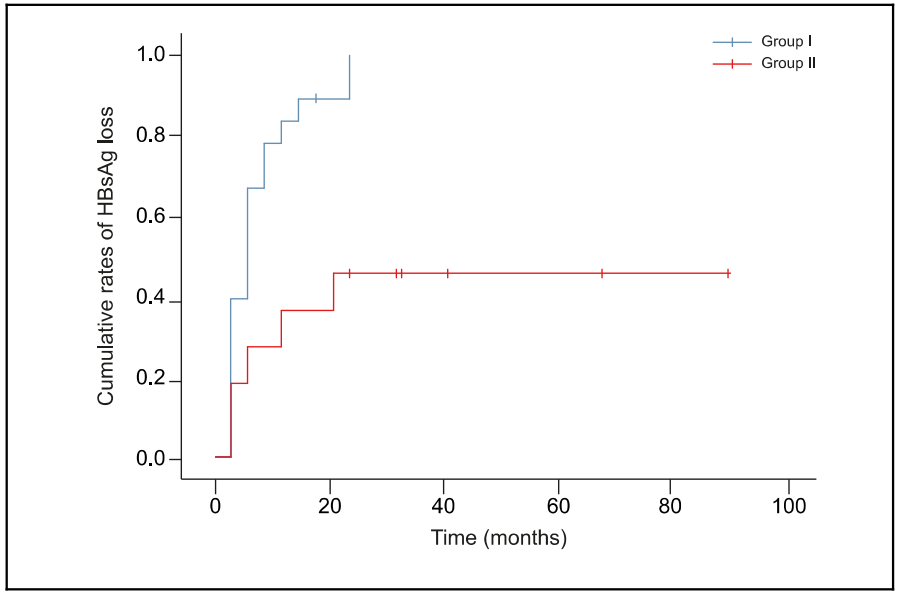
Early initiation of antiviral therapy contributes to a rapid and significant loss of serum HBsAg in infantile-onset hepatitis B

Shishu Zhu[1], Yi Dong[1], Limin Wang[1], Weiwei Liu[2], Pan Zhao[1,3,*]

J Hepatol 2019;71-871-875

- HBV-infected infants < 1 year of age
  - persistent elevation of alanine aminotransferase
  - high viral load





Cumulative rates of HBsAg loss

Month of treatment	3	6	9	12
Group I	39%	67%	78%	**83%**
Group II	18%	27%	27%	36%

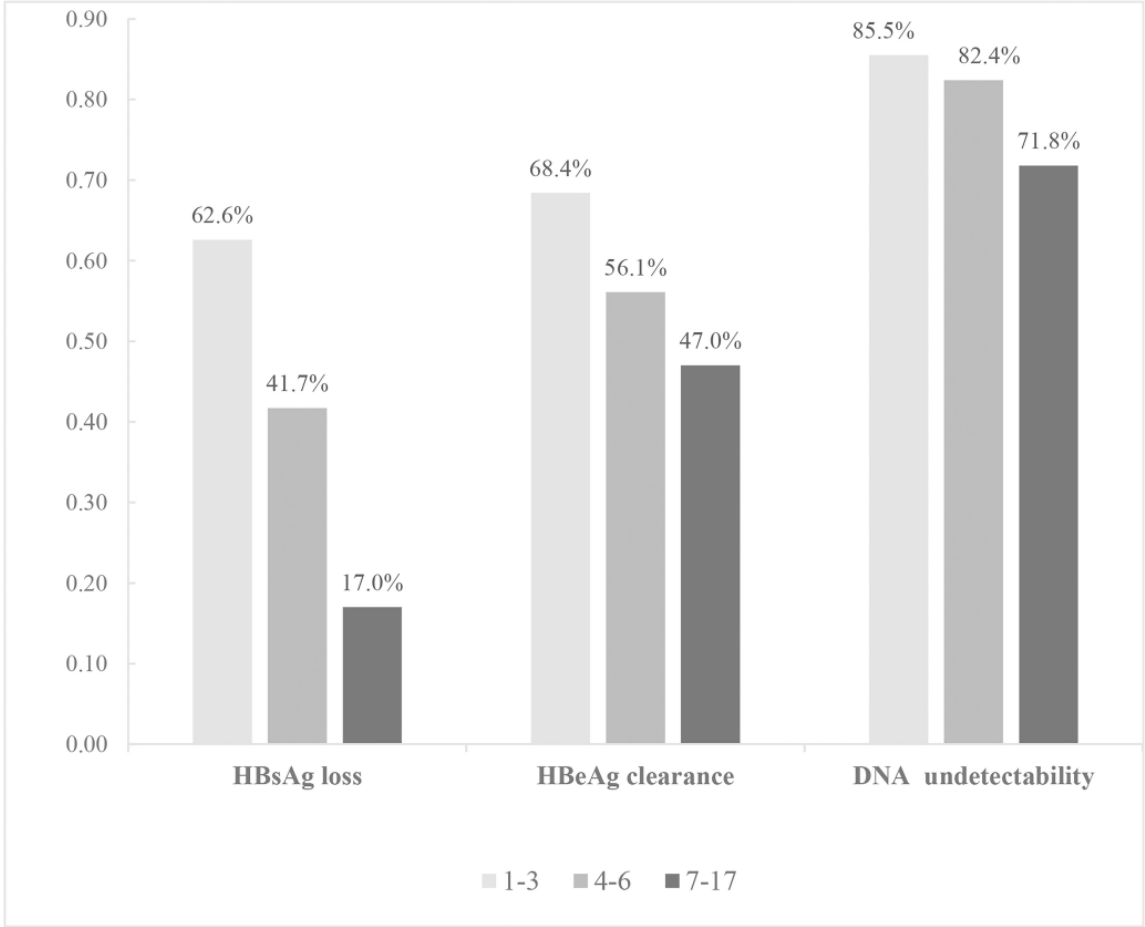
Age at treatment initiation predicts response in children with chronic hepatitis B

Aliment Pharmacol Ther 2023;58:866-873

Xiaoli Wu[1] | Zhenzhen Yao[2] | Xin Lai[2] | Yingping Gu[2] | Songxu Peng[2,3]

- 306 treatment-naïve immune tolerant children with CHB
  - 139 (45.4%) 1–3 years
  - 79 (25.8%) 4–6 years
  - 88 (28.6%) 7–17 years
- 285 combination therapy (interferon/peginterferon and entecavir)

- age at treatment negatively associated with
  - HBsAg loss
    - 1–3 years: HR = 5.07, 95% CI = 2.91–8.82;
    - 4–6 years: HR = 2.42, 95% CI = 1.31–4.46)
  - HBeAg clearance
    - 1–3 years: HR = 1.73, 95% CI = 1.18–2.53



CHB, chronic hepatitis B

Hepatitis C in children

Infectious

ESPGHAN updated guidelines

Treat all children (aged ≥3 years) with chronic infection

swallowability assessment is recommended before starting treatment

pangenotypic and genotype-specific DAA are equally recommended

pangenotypic, ribavirin-free and regimens with the shortest treatment duration are preferrable when alternatives are available

Hepatitis C in children

Infectious

Farmaci prescrivibili tramite portale AIFA >12 anni

Glecaprevir/pibrentasvir disponibile per <12 anni di età

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JPGN

POSITION STATEMENT

Hepatology

ESPGHAN recommendations on treatment of chronic hepatitis C virus infection in adolescents and children including those living in resource-limited settings

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Abstract

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease worldwide, with more than three million viraemic adolescents and children. Treatment of adults with HCV infection and HCV-related liver disease has advanced considerably thanks to development and improvements in therapy. Direct-acting antiviral regimens are safe and effective. Three regimens with pangenotypic activity (glecaprevir/pibrentasvir, sofosbuvir/velpatasvir and sofosbuvir/velpatasvir/voxilaprevir) and three regimens with genotype-specific activity (sofosbuvir/ribavirin, sofosbuvir/ledipasvir and elbasvir/grazoprevir) have been approved with age-specific limitation for treatment of children with chronic hepatitis C by the European Medicines Agency and the United States Food and Drug Administration. The World Health Organization has set the ambitious target to eliminate hepatitis C as a major public health threat by 2030 and based its actions against HCV on the large use of direct acting antivirals. These updated European Society for Pediatric Gastroenterology, Hepatology and Nutrition recommendations on treatment of hepatitis C describe the optimal therapeutic management of adolescents and children with HCV infection including specific indications for those living in resource-limited settings.

Disclaimer: The Hepatology Committee of the ESPGHAN: Benno Kohlmaier, Emer Fitzpatrick, Emmanuel Gonzales, Norman Junge, Sarah Mancell, Yael Mozer-Glassberg, Tudor Pop, Marianne Samyn, Xavier Stephenne, Aglaia Zellos. Please note that all the members of the Hepatology Committe of the ESPGHAN should be acknowledged as authors of the paper and indexed in Pubmed and other search engines.

Hepatitis in children: chronic infections

Results of the retrospective study of the SIGENP

Infectious

248 children

n 14

baseline

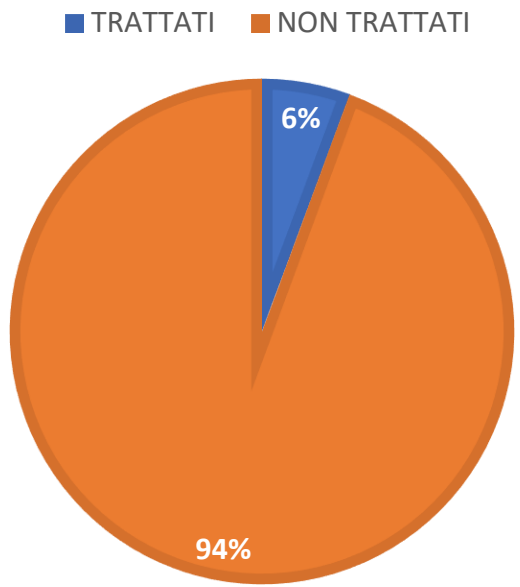
HBeAg+

- **209**
- **(83,8%)**

End of FU

HBeAg+

- **129**
- **(52,01%)**



Indolfi G, unpublished

Meyer

UNIVERSITÀ DEGLI STUDI FIRENZE

Conclusions

Challenges

- Complexity of the paediatric age
  - clinical
  - aetiological
  - epidemiological