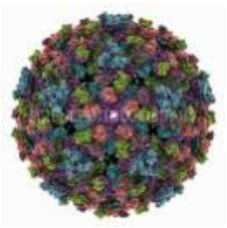
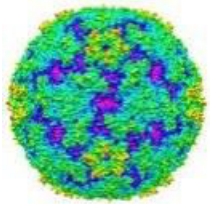
VIRUSES CAUSING MENINGITIS, ENCEPHALITIS AND MENINGO-ENCEPHALITIS (MEMe)

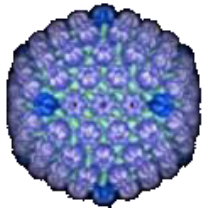
SALVACION R. GATCHALIAN, M.D.,
FPPS, FPIDSP, FPSMID



Chikungunya



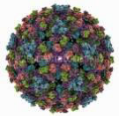
EV 71

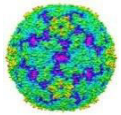


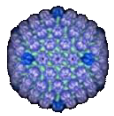
Viral Encephalitis

EMERGING VIRAL INFECTIONS (EID)

- Diseases that infected new hosts
- Spread into new geographic ranges
- Altered characteristics of pathogenensis
- Caused by agents not previously pathogeneic
- Taylor and colleagues reviewed risk factors for human disease
  - 1415 infectious organisms that are pathogenic to humans
  - 175 emerging
    - 44% are viruses and prions
  - Viruses have highest risk for emergence
  - 80% had primary non-human source (zoonotic)
  - 60% EID events are caused by zoonotic pathogens


Chikungunya


EV 71


Viral Encephalitis

Tyler K, Arch Neurol Aug 2009; 66(8): 939-948
Taylor et al, Philos Trans R Soc Lond B Biolo Sci 2001; 356 (1411): 983-989

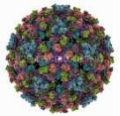
EMERGING INFECTIOUS DISEASES

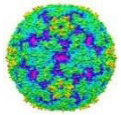
Highest concentration in US, Europe, Japan, and Southeast Asia

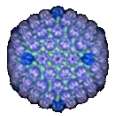
Predictive model identified “hotspots” due to zoonotic and vector-borne pathogens are in lower latitude developing countries (Tropical Africa, Latin America, Asia)

Olival and Daszak quantified viral EIDs affecting the nervous system

- 39% of viral EIDS cause severe neurologic symptoms, including encephalitis
- 10% rarely caused CNS symptoms


Chikungunya


EV 71


Viral Encephalitis

Tyler K, Arch Neurol Aug 2009; 66 (8): 939-948
Olival and Daszak J Neurovirol 2005; 11 (5): 441-446

VIRAL INFECITONS OF THE CNS

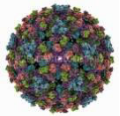
Leads to meningitis, meningo-encephalitis and encephalitis

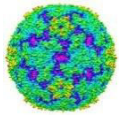
In practice, patients are diagnosed based on:

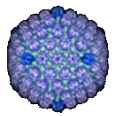
- Clinical manisfestations of brain dysfunction
- Laboratory or imaging evidence of inflammation

Acute life-threatening emergency

- Requires prompt treatment


Chikungunya


EV 71


Viral Encephalitis

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

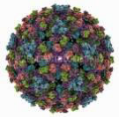
PATHOGENESIS

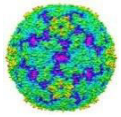
Direct invasion of brain tissue

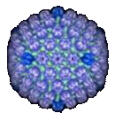
- Acute encephalitis
- Virus culture from brain or evidence of virus on histologic exam
- Occur as extension of viral meningitis, 2^0 to viremia, retrograde spread via peripheral nerves (rabies, HSV)

Provoke autoimmune response leading to acute disseminated encephalomyelitis (ADEM)

- Virus not detected or recovered from brain
- With history of illness 2-4 weeks prior to onset


Chikungunya


EV 71


Viral Encephalitis

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

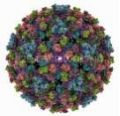
POSSIBLE INFECTIOUS ETIOLOGIES OF MENINGOENCEPHALITIS

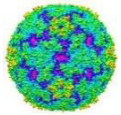
Viruses	Bacteria
Herpes Simplex Type 1	Fungi
Herpes Simplex Type 2	Parasites
Enteroviruses (echovirus, parechovirus, coxsackievirus A and B, poliovirus, and the numbered enteroviruses)	
Varicella Zoster Virus	
Epstein-Barr Virus	
Cytomegalovirus	
Human herpesvirus 6	
HIV	
Arboviruses (LaCrosse Virus, West Nile Virus, St. Louis encephalitis virus, Eastern and Western equine encephalitis virus, Japanese encephalitis virus)	
Rabies Virus,I nfluenza Virus, Measles Virus, Mumps Virus, Rubella Virus, Murray Valley Encephalitis Virus, Nipah Virus, Hendra Virus, Tick-Borne Encephalitis Virus, Powassan Virus, Herpes B Virus, Hepatitis E Virus, Creutzfeldt-Jakob Disease	

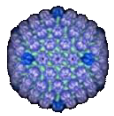
http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

EPIDEMIOLOGY of EV 71

- Non-polio enterovirus
- Major cause of encephalitis in children
- 78% in US occur Jun-Oct
- HFMD (Hand Foot Mouth Disease) common in children
  - Mild and self-limiting
  - In Asia, epidemics reported severe cases with complications
  - EV 71 cause of HFMD with high neurological disease and cardiopulmonary involvement


Chikungunya


EV 71


Viral Encephalitis

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

ENTEROVIRUS 71

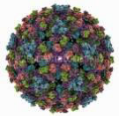
Virulent neurotropic enterovirus

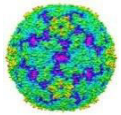
Mainly affects children < 5y

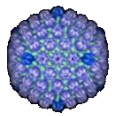
Transmitted by oral-fecal-route, direct contacts, saliva, fluids

Responsible of Hand, Foot and Mouth disease (HFMD)

- Usually benign and self-limiting:
  - Fever, sore throat, general malaise, painfull sore mouth/throat, rash (+blisters) hands and feet (see next slide1)
- Epidemic (seasonal): social burden, scholar and parents distress, school closures
- EV71 is responsible of 70-80% of HFMD and of most of serious cases (Coxsackie A responsible of most of remaining cases of HFMD – majority of those being CA16)


Chikungunya


EV 71

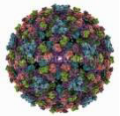

Viral Encephalitis

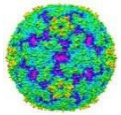
ENTEROVIRUS 71

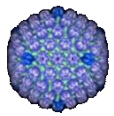
With EV71 possible (rare) serious complications :encephalitis, meningitis, acute flaccid paralysis or cardiac and pulmonary complications and deaths in children (see next slide2)

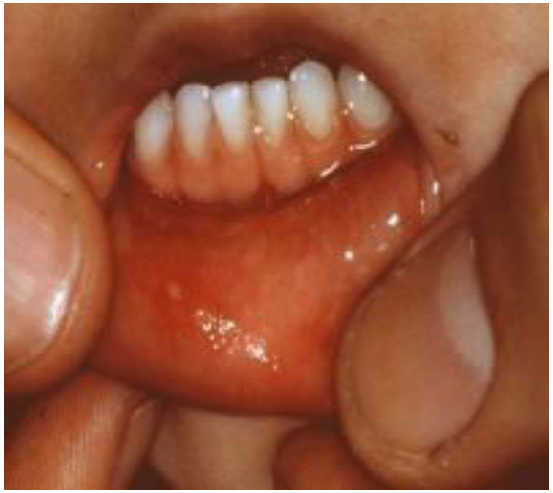
eg (Chang LY et al JAMA 2004): in 2001-2002 in an hospital in Taiwan 183 children were identified with infection with EV71:

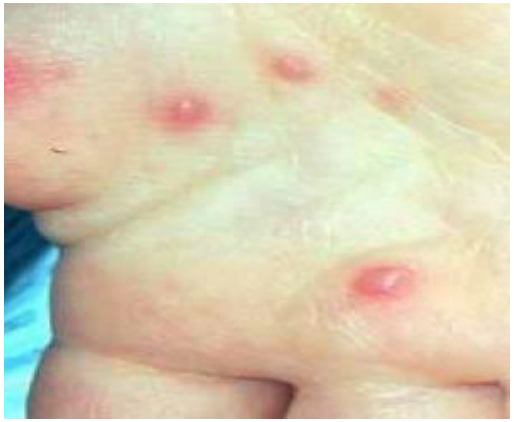
- 11 (6%) were asymptomatic
- 133 (73%) had uncomplicated illness (HFMD)
- 39 (21%) had complicated syndrome: CNS and cardiopulmonary failure
  - 13 (7%) long term sequela
  - 10 (5%) died
    (note: 87 adults from the same hospital were uneventfully affected)

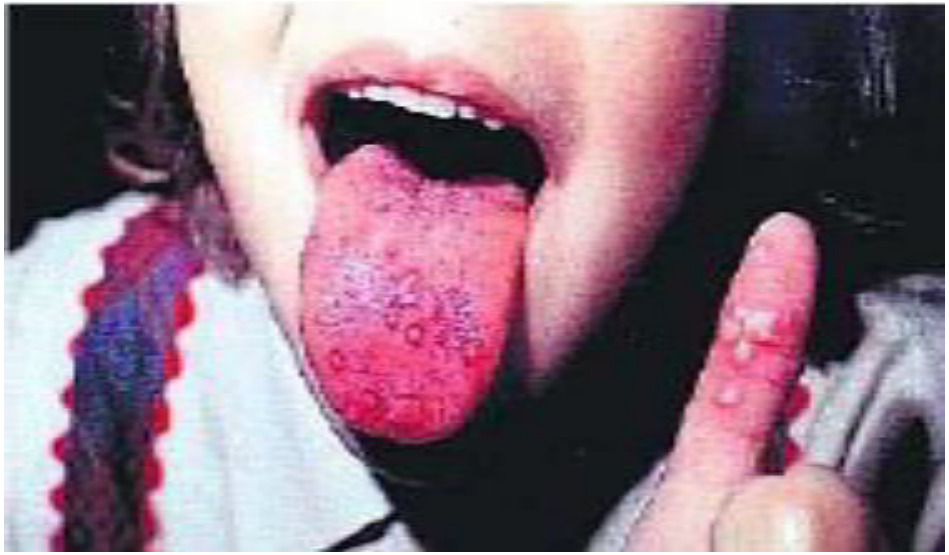

Chikungunya

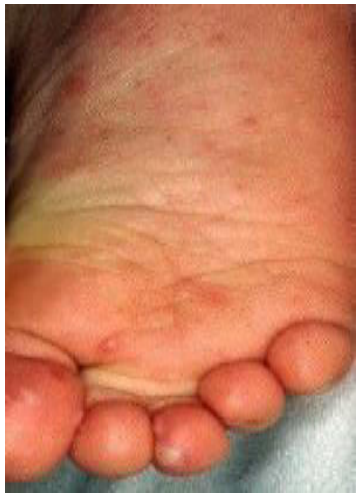

EV 71


Viral Encephalitis









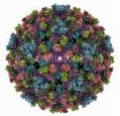
ENTEROVIRUS 71: EPIDEMIOLOGY

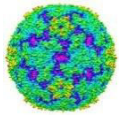
EV 71 was first identified in US California in 1969 (encephalitis in a child)

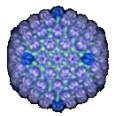
Epidemics with serious neurological disorders occurred in Bulgaria, Hungary in the seventies

In last decades several large outbreaks have spread across Asia:

- China:
  - No epidemics 1999-2006 but small sporadic inland or coastal outbreaks with (for Shenzhen) a few neurological cases but no fatalities reported
  - 17 deaths and 80,000 cases in 2007
  - 44 deaths and 176,000 infections in 2008 (to date): media coverage


Chikungunya


EV 71

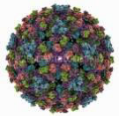

Viral Encephalitis

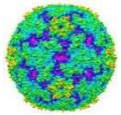
ENTEROVIRUS 71: EPIDEMIOLOGY

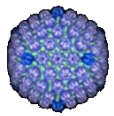
Continued….

In last decades several large outbreaks have spread across Asia:

- Singapore (mid year 2008: 4,839 400 inhabitants; 671 300<14y)
  - Almost annual outbreak (see slide) and increasing prevalence:
    - 6403 cases in 2004; 15257 in 2005, 15299 in 2006, 20012 in 2007, 29686 cases in 2008 with 2 encephalitis and 1 death in August 08 (first since 2000-2001)[1]
  - 9649 cases in 2009 (up to 27 June)[2]
  - The predominant strain isolated during the epidemic period was CA16 in 2005 and 2007, and EV71 in 2006 (20.5%) and 2008 (33.2%)[3]


Chikungunya


EV 71


Viral Encephalitis

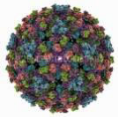
1. Weekly Infectious Disease Bulletin. Vol. 5 No. 53 2008. Ministry of Health, Singapore.
2. Weekly Infectious Disease Bulletin. Vol. 6 No. 25 2009. Ministry of Health, Singapore.
3. Epidemiological News Bulletin. Oct-Dec 2008 Vol. 34 No. 4. Ministry of Health, Singapore.

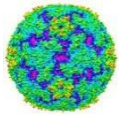
ENTEROVIRUS 71: EPIDEMIOLOGY

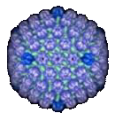
Continued….

In last decades several large outbreaks have spread across Asia:

- Taiwan:
  - 78 deaths in 1998 (405 severe complications and 1.5M children affected)[1]
  - almost annual outbreaks
  - More than 200,000 cases in 2008 (to date)?: large media coverage
  - In 2008, 344 cases of EV71 infection with severe complication, including 12 deaths[2]
- Malaysia:
  - 5999 cases and 42 deaths in 1997, subsequent outbreak in 2000, 2002, 2005, and 2006[3]
  - 5,141 cases (5 deaths) in 2006[3] (to be compared with 17,147 cases and one death for dengue fever)
- Vietnam:
  - 764 cases of HFMD in 2005, 173 with EV71 (51 with neurological disease and 3 deaths)[4]
  - 12 HFMD deaths, 2,800 cases in 2008 (May)[5]
  - Increase in cases of HFMD in 2009 (Apr)[6]


Chikungunya


EV 71


Viral Encephalitis

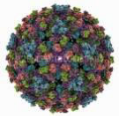
1. Ho M et al. An epidemic of enterovirus 71 infection in Taiwan. *New England Journal of Medicine* 1999. 341(13):929-935.
2. Taiwan domestic epidemic of infectious disease report. Jan 2009. Taiwan CDC.
3. Communicable disease surveillance, Disease Control Division, Ministry of Health Malaysia. http://www.dph.gov.my/survelans/
4. Phan VT et al. Epidemiologic and virologic investigation of hand, foot and mouth disease, southern Vietnam, 2005. *Emerging Infectious Disease*, 2007, 13(11):1733-1741
5. The Jakata Post, http://www.thejakartapost.com/news/2008/05/23/vietnam-warns-hand-foot-and-mouth-disease-spreading-among-children.html
6. National Travel Health Network and Centre. http://www.nathnac.org/pro/clinical_updates/hfmd_220409.htm

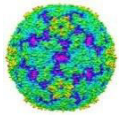
ENTEROVIRUS 71: EPIDEMIOLOGY

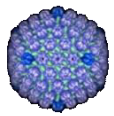
Continued….

In last decades several large outbreaks have spread across Asia:

- **Hong Kong:**
  - **one monoplegia in 1987[1], one death in 2001[2]**
  - **only tenths of EV71 cases reported yearly 2004-2007: 35 cases in 2004, 8 cases in 2005, 16 cases in 2006, 12 in 2007[3]**
  - **98 cases in 2008 including 8 cases with severe complications and 1 death[3]**
  - **49 cases of HFMD (21 EV71 infection, including 1 case with severe complication and 1 death) In 2009 (up to 2nd Jul)[3]**
- **Korea: outbreak in 2000[4]**
  - **1 death and 1 toddler left brain dead in 2009 (June)[5]**


Chikungunya


EV 71


Viral Encephalitis

1. Samuda GM et al. Monoplegia caused by enterovirus 71: an outbreak in Hong Kong. Pediatr Infect Dis J 1987;6:206-8
2. Ng DKK et al. First fatal case of enterovirus 71 infection in Hong Kong. *Hong Kong Medical Journal* 2001; 7(2):193-196
3. EV Scan (Week 27, 2009). Centre for Health Protection, Department of Health Hong Kong
4. Jee YM et al. Genetic analysis of the VP1 region of human enterovirus 71 strains isolated in Korea during 2000. Arch. Virol 2000;148:1735-1746.
5. The Korea Times. http://www.koreatimes.co.kr/www/news/nation/2009/06/113_46311.html

Taiwan 1998-2006

Table 1 Number of cases of severe and fatal enterovirus infections in Taiwan from 1998 to 2006

Year	Number of severe cases	Number of fatal cases (severe case-fatality rate)	EV71 number (%) among the fatal cases
1998	405	78 (19%)	34 (44%)
1999	35	9 (26%)	1 (11%)
2000	291	41 (14%)	25 (61%)
2001	393	58 (15%)	27 (47%)
2002	162	30 (19%)	8 (27%)
2003	70	8 (11%)	4 (50%)
2004	50	5 (10%)	5 (100%)
2005	142	16 (11%)	7 (44%)
2006	11	0	0
Total	1559	245 (15.7%)	111 (45.3%)

Data from CDC, Taiwan.

Chang LY Enterovirus 71 in Taiwan. Pediatr Neonatol 2008;49(4):103-112

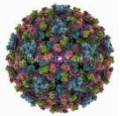
Hong Kong 2004-2008

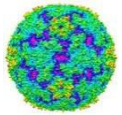
Annual number of HFMD outbreaks and EV71 cases in Hong Kong

Year 年份	Number of HFMD institutional outbreaks (persons affected) 手足口病院舍爆發數目^ (受影響人數)	Number of EV71 cases 腸病毒７１型個案數字	Number of EV71 cases with severe complication 有嚴重併發症的腸病毒７１型個案數字	Number of fatal cases 死亡個案數字
2004	159 (1046)	35	0	0
2005	90 (656)	8	0	0
2006	236 (1744)	16	1	0
2007	157 (1081)	12	0	0
2008	167 (967)	98	8	1

^Statistics on HFMD also includes herpangina 手足口病統計數字包括疱疹性咽峽炎

EV Scan (Week 27, 2009). Centre for Health Protection, Department of Health Hong Kong


Chikungunya


EV 71

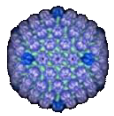
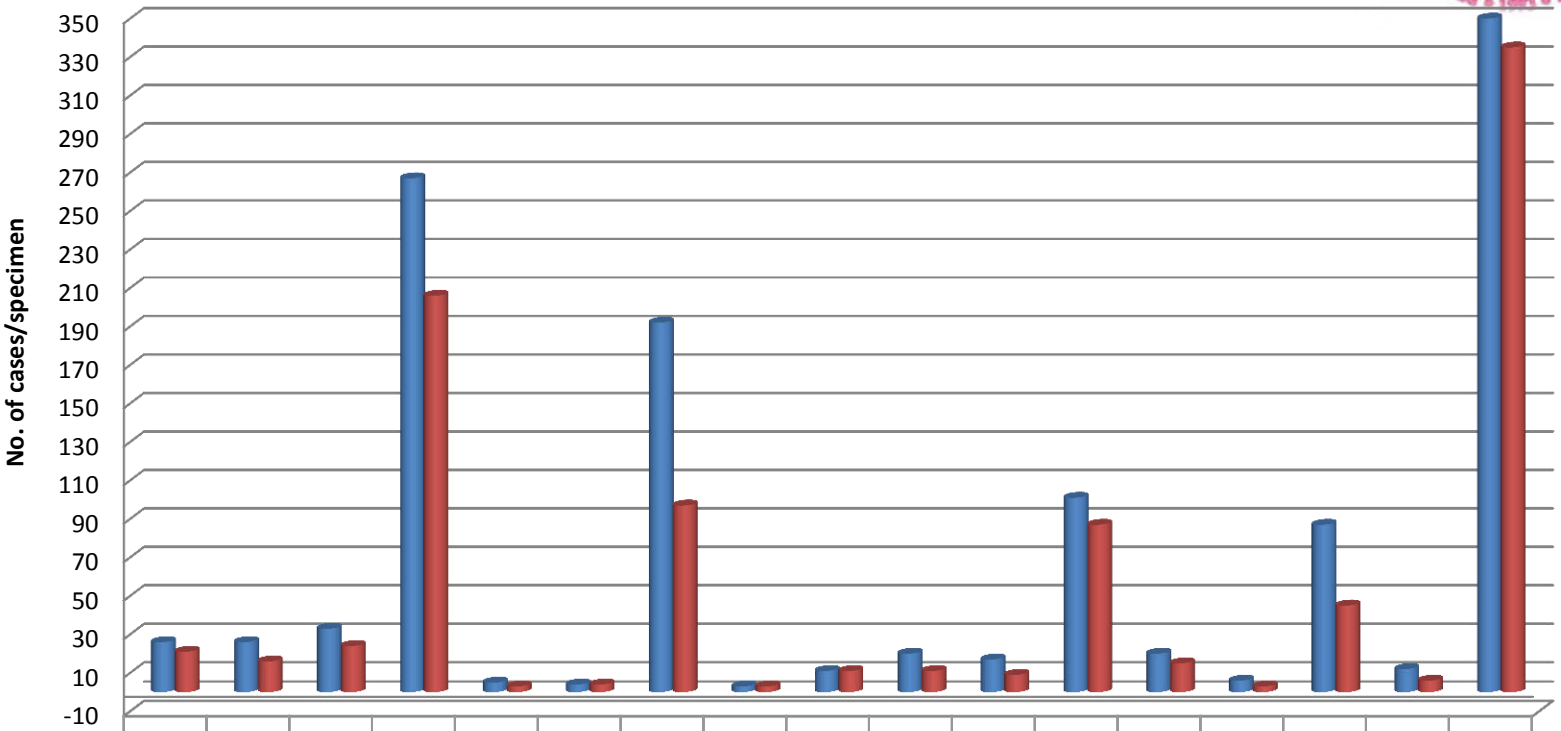
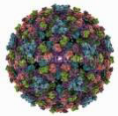
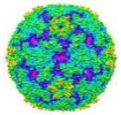

Viral Encephalitis

Figure 1. Distribution of Cases and Specimen by Region, July-Dec 2012



	1	2	3	4A	4B	5	6	7	8	9	10	11	12	ARMM	CAR	CARAGA	NCR
# Specimen Received	26	26	33	267	5	4	192	3	11	20	17	101	20	6	87	12	385
Cases	21	16	24	206	3	4	97	3	11	11	9	87	15	3	45	6	335


Chikungunya


EV 71

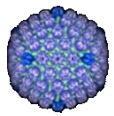
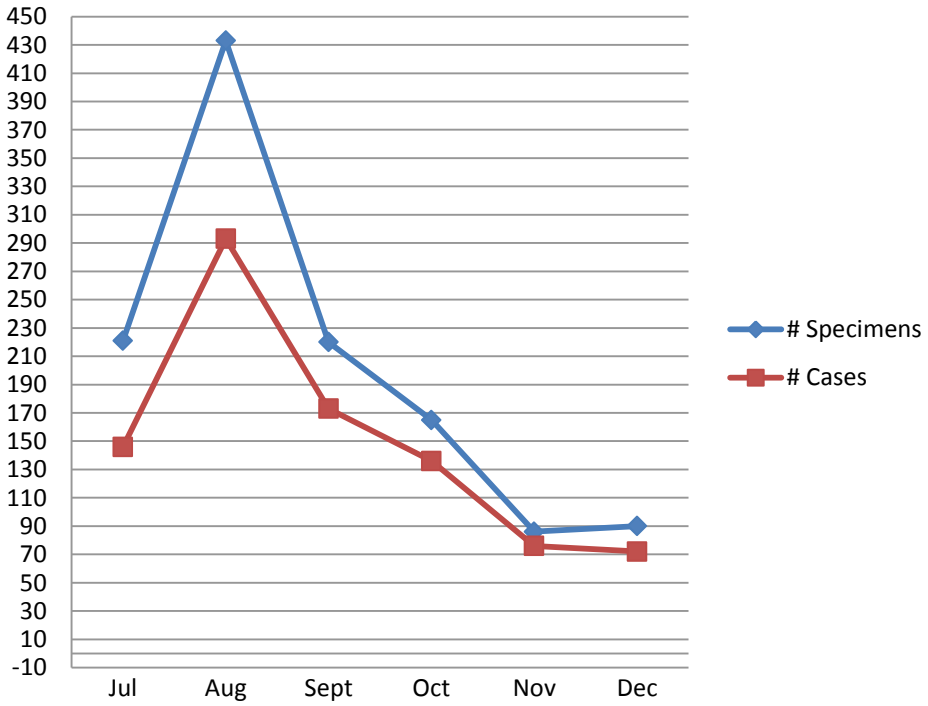
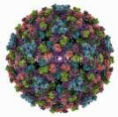

Viral Encephalitis

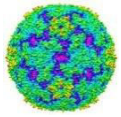
Figure 3. Distribution of Cases/Specimen by month

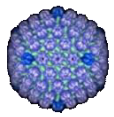


Enterovirus Results (July-Dec 2012)

Results by Case	No. of cases	Percentage
ENTEROVIRUS POSITIVE	671	75.5%
EV-71 POSITIVE	22	3.3%
NEGATIVE	173	19.5%
NOT TESTED	45	5%
Grand Total	889	

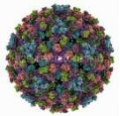

Chikungunya

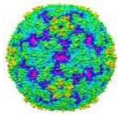

EV 71

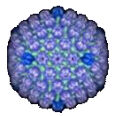

Viral Encephalitis

EPIDEMIOLOGY OF JAPANESE B

- One of leading cause of acute encephalopathy in the tropics
- Worldwide, 50,000 cases
- 15,000 (30%) die
- Mosquito-borne viral infection of the CNS (Culex tritaeniorrhynchus)
- Neurotropic flavivirus
- Transmitted among birds, pigs, and other vertebrate hosts by vector-borne mosquito, culex species
- Humans dead end hosts and infected when encroach on enzoonotic cycle
- Major public health problem in Asia


Chikungunya

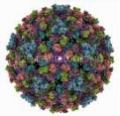

EV 71

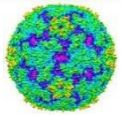

Viral Encephalitis

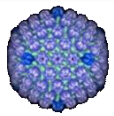
Solomon et al j Neurol Neurosurg Pscychiatry2000; 68: 405-415
Ooi et al Clin Infect Dis Aug 15 2008; 47

EPIDEMIOLOGY OF JAPANESE B

- Mainly a disease of children in rural areas
- Acute Case Fatality Rate 30%
- 50% survivors with neurologic sequelae
- After monsoon rains, mosquito breed and as they increase in number, carriage also increases
- Viremia is brief and titers low
- Asia, infection occurs in children and early adulthood


Chikungunya

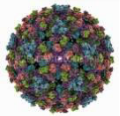

EV 71

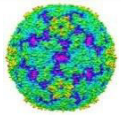

Viral Encephalitis

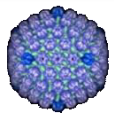
Solomon et al j Neurol Neurosurg Pscychiatry2000; 68: 405-415
Ooi et al Clin Infect Dis Aug 15 2008; 47

EPIDEMIOLOGY OF CHIKUNGUNYA VIRUS

- Acute febrile illness caused by arthropod-borne aphavirus, Family *Togaviridae Chikungunya virus* (CHIKV)
- Recognized as a human pathogen during 1950s in Africa
- Cases identified since then in Africa and Asia
- Transmitted to humans via bite of infected *Aedes* species mosquito
- Circulates in a sylvatic cycle between forest dwelling *Aedes* species mosquitoes and non-human primates
- In urban centers of Africa and Asia, virus can circulate between mosquitoes and naive human similar ot dengue viruses


Chikungunya


EV 71


Viral Encephalitis

Staples et al Clin Inf Dis Sept 2009; 49: 942-8
Mohan et al indian J Dermatol 2010 Jan-Mar; 55 (1): 54-63

EPIDEMIOLOGY OF CHIKUNGUNYA VIRUS

2 main vectors:

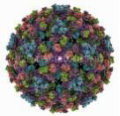
- *Aedes aegypti*
- *Aedes albopictus*

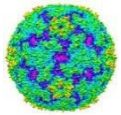
Resurgence drawn global attention due:

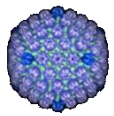
- Explosive onset
- rapid spread
- high morbidity
- myriad of clinical manifestations

2006 onwards, emerged in non-endemic areas as important disease in returning travellers

- Sentinels
- Transporters
- Transmitters


Chikungunya


EV 71


Viral Encephalitis

Staples et al Clin Inf Dis Sept 2009; 49: 942-8
Mohan et al indian J Dermatol 2010 Jan-Mar; 55 (1): 54-63

EPIDEMIOLOGY OF CHIKUNGUNYA VIRUS

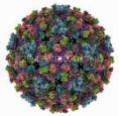
Displays secular, cyclical and seasonal trends

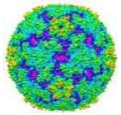
Epidemics are explosive outbreaks interspersed by periods of disappearance from several years to decades

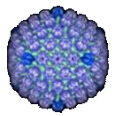
- Reason unknown
- Humans are reservoir
- Interpandemics vertebrates (monkeys, rodents, birds)

No evidence of tranovarial transmission of CHIKV in mosquitoes

Vertical maternal-fetal transmission documented


Chikungunya


EV 71


Viral Encephalitis

Staples et al Clin Inf Dis Sept 2009; 49: 942-8
Mohan et al indian J Dermatol 2010 Jan-Mar; 55 (1): 54-63

Acta Medica Philippina

The National Health Science Journal
Published by the University of the Philippines Manila,
the Department of Science and Technology and
the Philippine Council for Health Research and Development

ACTA MEDICA PHILIPPINA

Isolation of Chikungunya Virus in the Philippines

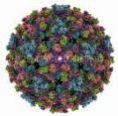
(Received February 10, 1969)

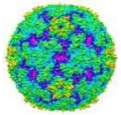
Lourdes E. Campos, M.D., M.P.H., Adelina San Juan, B.S. Hygiene,
Linda C. Cenabre, B.S. Hygiene
Department of Medical Microbiology, Institute of Hygiene
and Elena F. Almagro, B.S. Hygiene
Medical Research Laboratory
Department of Medicine, College of Medicine

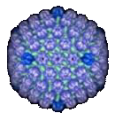
SUMMARY

The isolation of 15 viral agents in suckling mice from 26 serum samples of cases charaterized by fever, rash and severe and lingering joint pains is presented. Eight hemagglutinating isolates were identified by hemagglutination-inhibition test. Seven of them were identified as chikungunya virus and one, a group B arbovirus, most probably a dengue virus. The immunologic responses noted in the patients confirm the identity of the isolates.

- **1st reported cluster in the Philippines in 1967. Testing confirmed presence of Chikungunya virus in the outbreak samples.**


Chikungunya


EV 71


Viral Encephalitis

EPIDEMIOLOGIC AND HISTORIC CLUES TO THE ETIOLOGY OF ENCEPHALITIS IN CHILDREN

Epidemiologic Clues	Potential Etiologies
Age (0 to 28 days)	Infectious: CMV, HSV-2 or HSV-1 Rubella Virus
Season: Summer Late Summer/Fall Winter Infection in Horses, birds Blood Transfusion or Transplant recipient Immunodeficiency	 Enterovirus, Free living amebae Arbovirus Postinfectious encephalitis in countries with low rates of MMR immunization Arbovirus CMV, EBV, HIV, rabies, tick-borne encephalitis, WNV CMV, enterovirus, HHV6, HSV, VZV, WNV
Historical Clues	
Rash: Vesicular Hand, foot, mouth Erythematous macules and papules with cephalocaudad spread Maculopapular Maculopapular/petechial begins on ankles and wrists	HSV, VZV, enterovirus (Hand, foot, and mouth disease), herpes B virus Enterovirus Measles WNV Rocky Mountain spotted fever
Exposures: Mosquitoes Ticks Animal bite/exposure (dog, bat, cat, birds, livestock, others) Blood transfusion or transplant recipient Recent Infectious Illness	 Arbovirus Borrelia burgdorferi, Powasan virus, Rickettsia rickettsii, tick-borne encephalitis Rabies, arboviruses, cat scratch disease, Q fever CMV, EBV, HIV, rabies, tick-borne encephalitis, WNV ADEM
Recreational Activity: Swimming / Spelunking / Sexual Activity	 Enteroviruses, free-living amebae / Rabies / HIV

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

TRAVEL HISTORY AND POSSIBLE ETIOLOGIC AGENT(S) OF VIRAL ENCEPHALITIS

Travel	Possible Infectious Agent(s)
Africa	Rabies, West Nile Virus, Plasmodium Falciparum, Trypanasoma brucei gambiense, T. Brucei rhodesiense
Australia	Murray Valley encephalitis virus, Japanese encephalitis virus, Hendra virus
Central America	Rabies virus, Eastern equine encephalitis virus, Western equine encephalitis virus, Venezuelan encephalitis virus, St. Louis encephalitis virus, Rickettsia rickettsii, P. Falciparum, Taenia solium
Europe	West Nile Virus, Tick-borne encephalitis virus, Borrelia burgdorferi, Anaplasma phagocytophilum
India, Nepal	Rabies Virus, Japanese Encephalitis virus, P. Falciparum
Middle East	West Nile Virus, P. Falciparum
Russia	Tick-Borne encephalitis virus
South America	Rabies virus, Eastern equine encephalitis virus, Western equine encephalitis virus, Venezuelan encephalitis virus, St. Louis encephalitis virus, Rickettsia rickettsii, Bartonella bacilliformis (Andres mountain) . Falciparum, Taenia solium
Southeast Asia, China, Pacific Rim	Japanese Encephalitis Virus, Tickborne Encephalitis Virus, Nipah Virus, P. Falciparum, Gnathostoma species, Taenia solium

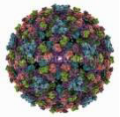
http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

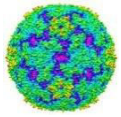
CLINICAL MANIFESTATIONS

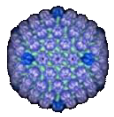
Encephalitis causes neurologic dysfunction with broad range of presentation

Clinical manifestation vary

- Portions of CNS affected
- Pathogenic agent
- Host factors
  - Clinical features of viral infection at specific sites of CNS


Chikungunya


EV 71

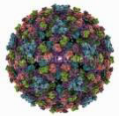

Viral Encephalitis

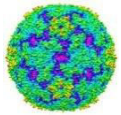
http://www.uptodate.com/contents/acute-viral-encephalitis-in -children-and-adolescents 2/18/2013

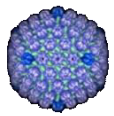
Tyler K, Arch Neurol Aug 2009; 66 (8): 939-948
Solomon et al j Neurol Neurosurg Pscychiatry2000; 68: 405-415
Ooi et al Clin Infect Dis Aug 15 2008; 47
Lee et al Pedia Infect Dis J Oct 2009;28 (10):904-910
Wi-SunRyu et al J Clin Micro Jul 2010;48 (7): 2490-2494

CLINICAL CLUES FOR VIRAL INFECTIONS OF THE CNS IN CHILDREN

Etiology	Frequency of Meningitis vs Encephalitis		Potential Clues
	Meningitis	Encephalitis	
Enteroviruses (EV71)	Common	Rare	Rash - popular & petechial with diffuse erythema in trunk and limbs.
			Faucial rush of blisters with haloes of inflammation
			Truncial ataxia, myoclonus, intertion tremor
			Impaired consiousness
			Pulmonary edema
			Pharyngitis, croup, bronchiolitis, pneumonia


Chikungunya

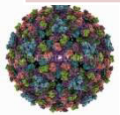

EV 71

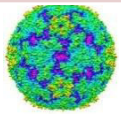

Viral Encephalitis

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

CLINICAL CLUES FOR VIRAL INFECTIONS OF THE CNS IN CHILDREN

Etiology	Frequency of Meningitis vs Encephalitis		Potential Clues
	Meningitis	Encephalitis	
Japanese B	rare	common	Non specific febrile illness (coryza, diarrhea, rigor), headache, vomiting
			Reduced level of conciousness
			convulsion
			Abnormal behavior (older children and adults)
			Dull, flat mask-like facies with wide unbinking eys, tremor, generalized hypertonia, rigidity
			Accute flaccid paralysis


Chikungunya

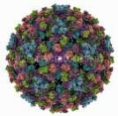

EV 71

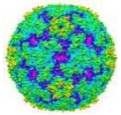

Viral Encephalitis

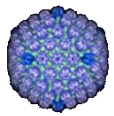
http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

CLINICAL CLUES FOR VIRAL INFECTIONS OF THE CNS IN CHILDREN

Etiology	Frequency of Meningitis vs Encephalitis		Potential Clues
	Meningitis	Encephalitis	
Chikungunya Fever	Not common	Not common	Abrupt, sudden onset of fever
			Arthralgias, myalgia
			Skin rash
			Headache, throat discomfort, abdominal pain, constipation
			Conjunctival suffusion, persistent conjunctivitis, cervical or generalized lymphadenopathy

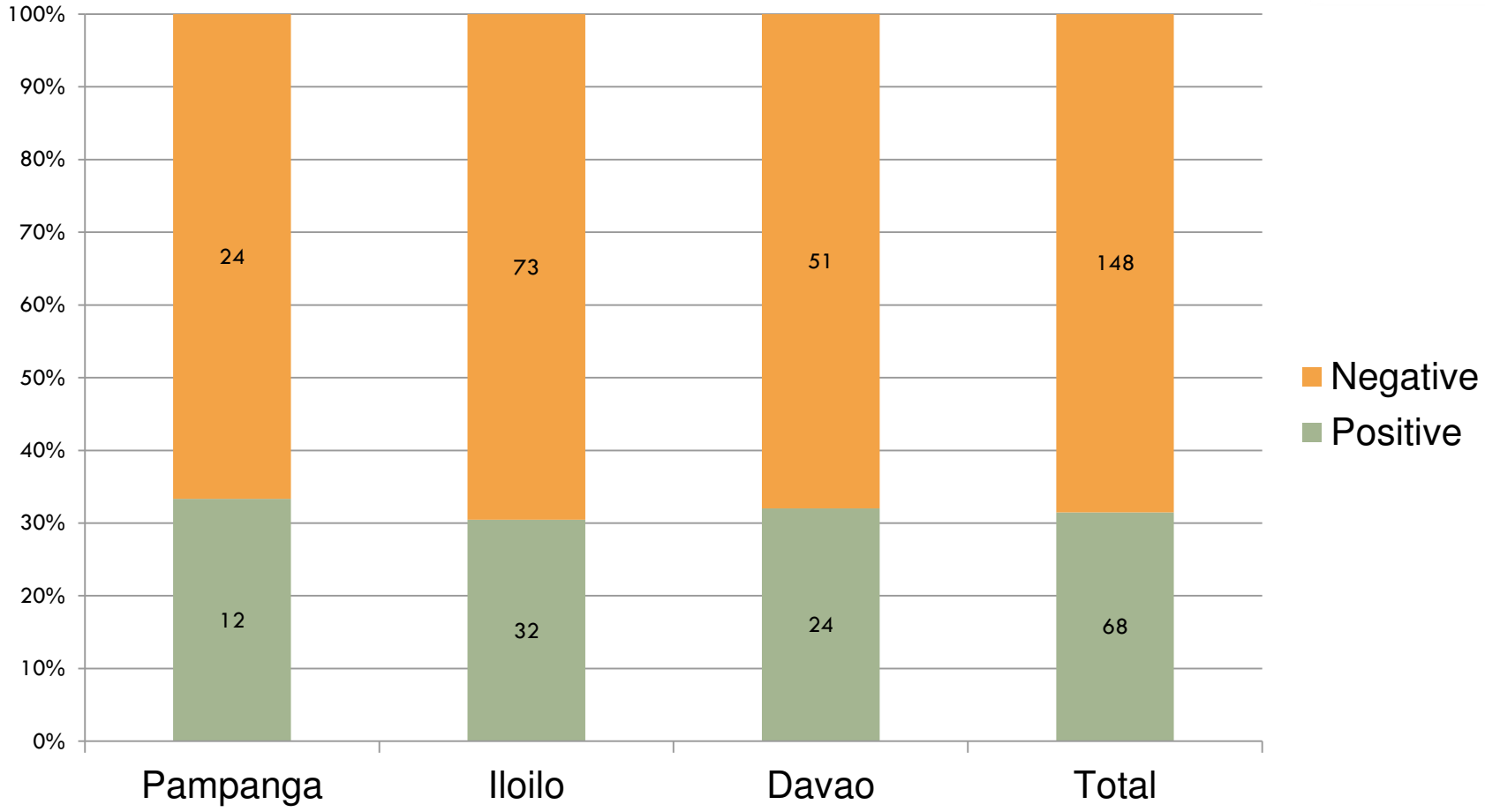

Chikungunya


EV 71

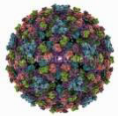

Viral Encephalitis

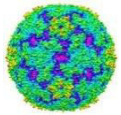
http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

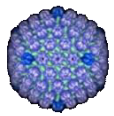
Percentage of CHIKV among DEN Negative pediatric patients from 2009-2010 in 3 sentinel sites (N=216)



Sy et al, 2011 (unpublished)


Chikungunya

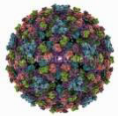

EV 71

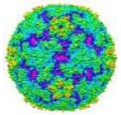

Viral Encephalitis

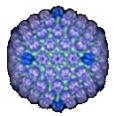
RITM EXPERIENCE IN 2012

- **Brought about by the outbreaks in 2011, RITM through the support of DOH, has begun providing IgM testing services for Chikungunya**
- **A total of 990 referrals for Chikungunya IgM Testing were received at the NRL for Dengue and other Arboviruses (this includes samples from clusters of cases as well as routine diagnostic samples)**

Chikungunya IgM Testing 2012			
Positive	Equivocal	Negative	Total
562 (56.7%)	67 (6.2%)	367 (37.1%)	990


Chikungunya

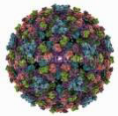

EV 71

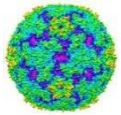

Viral Encephalitis

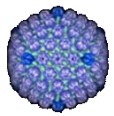
CAPTURED THROUGH MEASLES SURVEILLANCE

- From June-September 2012, cases in several regions with fever and rash were investigated under the measles surveillance.
- Cases had pronounced joint symptoms/body aches and occurred generally in the more elderly population.
- Out of 43 measles negative cases, 30 (70%) were positive for CHIKV IgM, 5 (12%) were equivocal, and 8 (18%) negative.

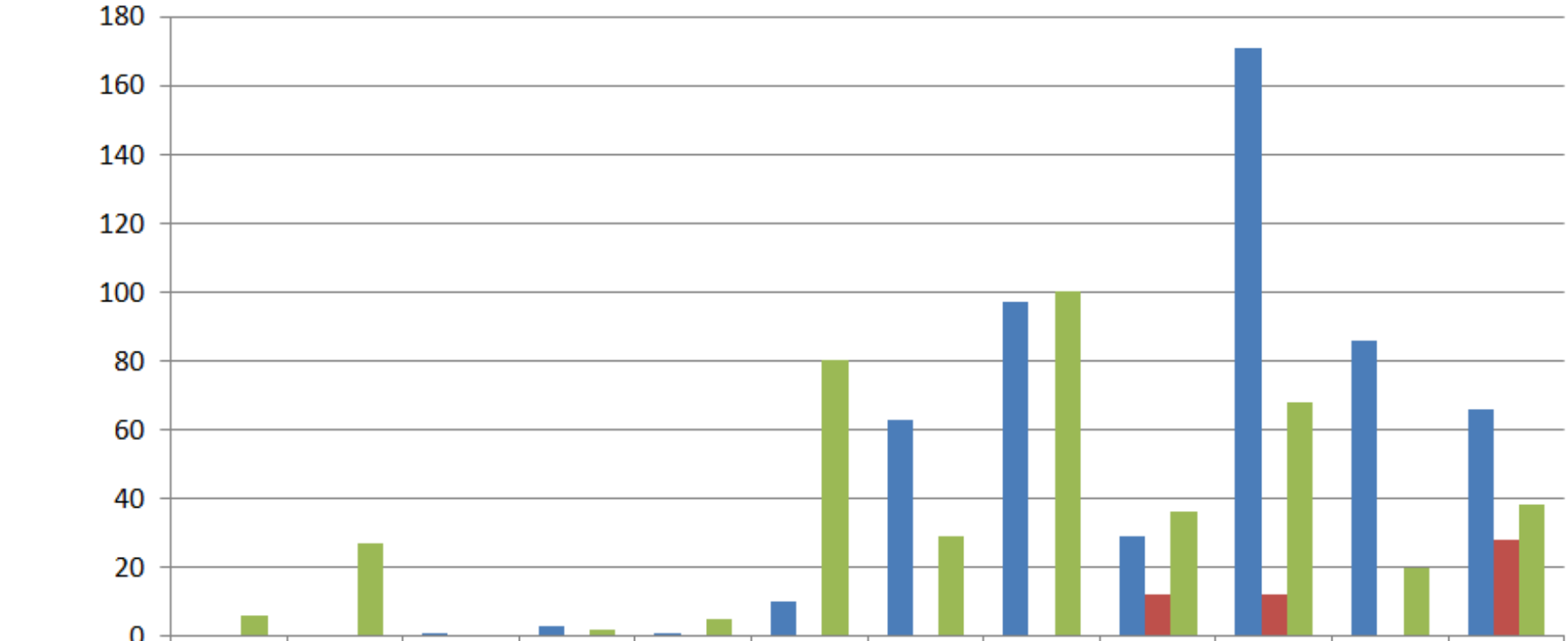
Chikungunya IgM Testing of Measles Negative Cases			
Positive	Equivocal	Negative	Total
30 (70%)	5 (12%)	8 (18%)	43


Chikungunya


EV 71

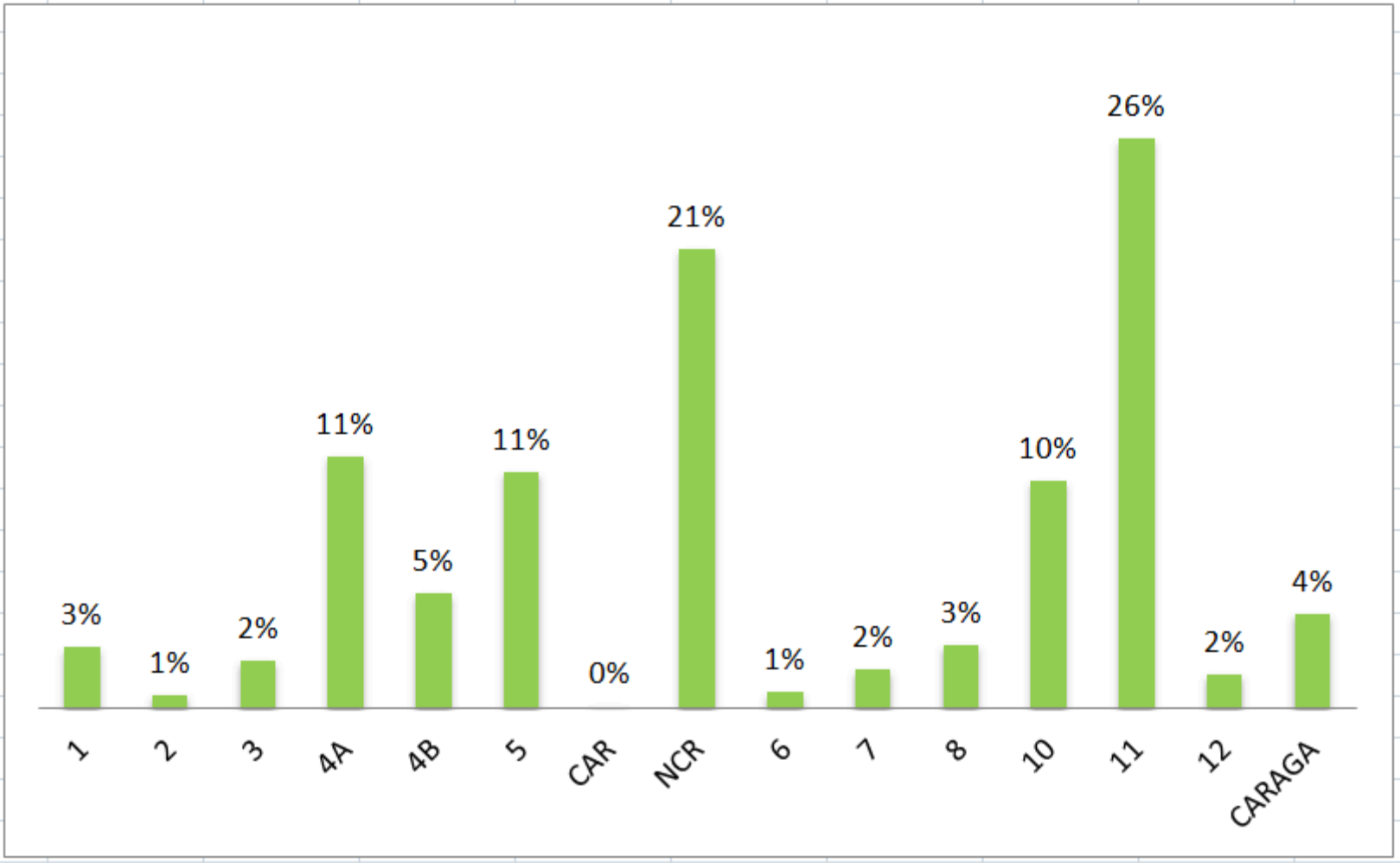

Viral Encephalitis

RITM EXPERIENCE IN 2012
(Distribution over Space and Time)

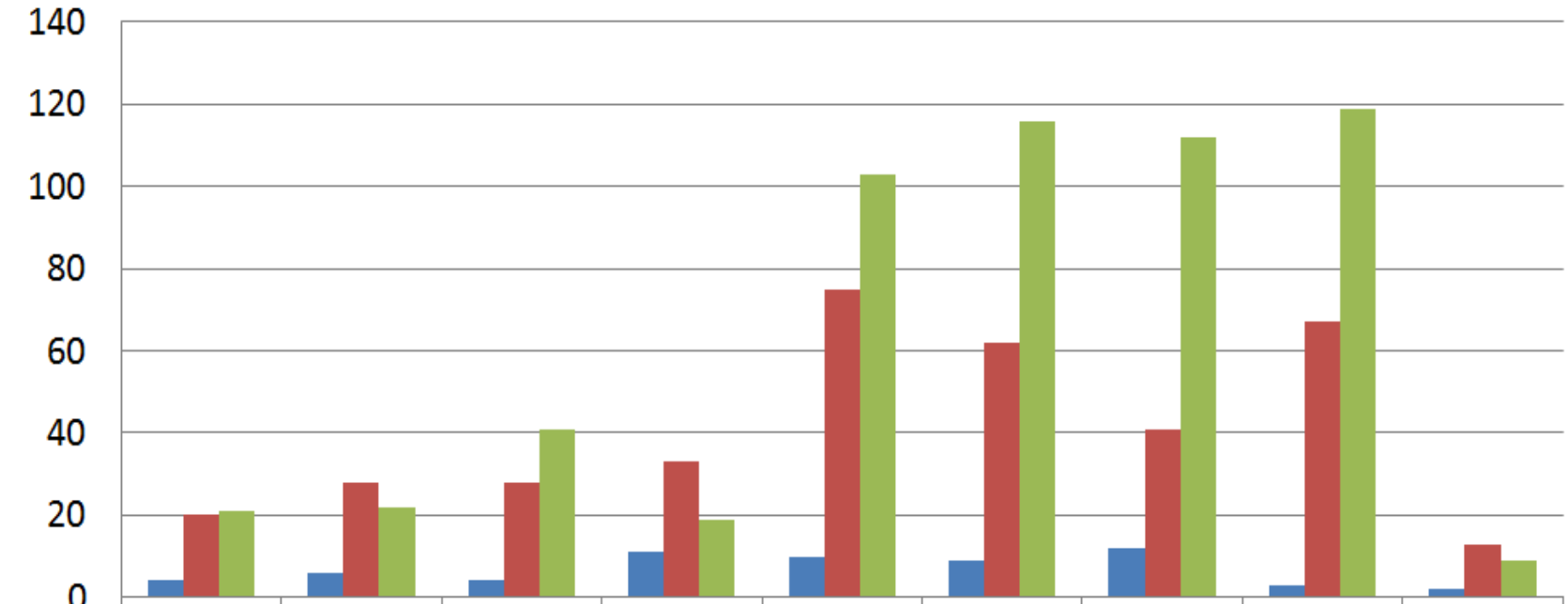


	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Luzon	0	0	1	3	1	10	63	97	29	171	86	66
Visayas	0	0	0	0	0	0	0	0	12	12	0	28
Mindanao	6	27	0	2	5	80	29	100	36	68	20	38

RITM EXPERIENCE IN 2012
(Distribution across Regions)

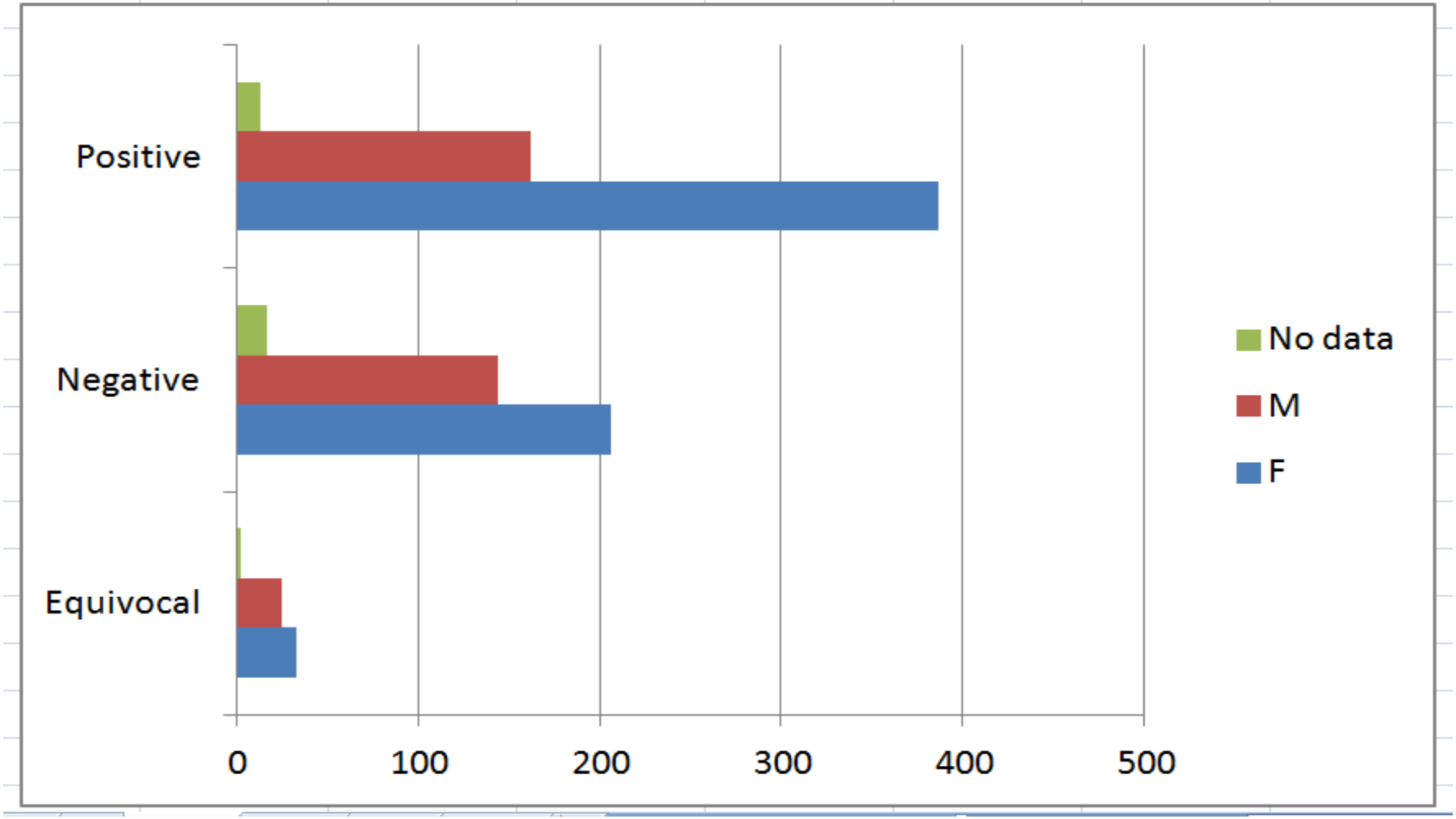


RITM EXPERIENCE IN 2012
(Age Distribution)



	0 to 5	5 to 10	11 to 15	16 to 20	21 to 30	31 to 40	41 to 50	> 50	No data
Equivocal	4	6	4	11	10	9	12	3	2
Negative	20	28	28	33	75	62	41	67	13
Positive	21	22	41	19	103	116	112	119	9

RITM EXPERIENCE IN 2012
(Sex distribution)



COMPARISON BETWEEN CHIKUNGUNYA AND DENGUE FEVER

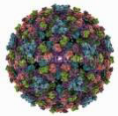
	CHIKUNGUNYA	DENGUE
Fever	Common	Common
Rash	D1-D4	D5-D7
Retroorbital pain	Rare	Common
Arthralgia	Constant	Rare
Arthritis	Common, edematous	Absent
Myalgia	Common	Common
Tenosynovitis	Common	Absent
Hypotension	Possible	Common, D5-D7
Minor Bleeding	Rare	Common, D5-D7
Outcome	Persistent arthralgia for months to years, M2-M3 Possible Raynaud/tenosynovitis	Possible Fatigue for weeks
Thrombocytopenia	Early and mild	Delayed and possibly deep

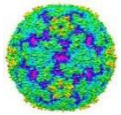
Staples et al Clin Inf Dis Sept 2009; 49: 942-8

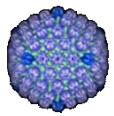
ChikV v DENV LABORATORY PROFILE

Laboratory features	Chikungunya virus infection	Dengue virus infection
Leukopenia	++	+++
Neutropenia	+	+++
Lymphopenia	+++	++
Elevated hematocrit	-	++
Thrombocytopenia	+	+++

Staples et al Clin Inf Dis Sept 2009; 49: 942-8

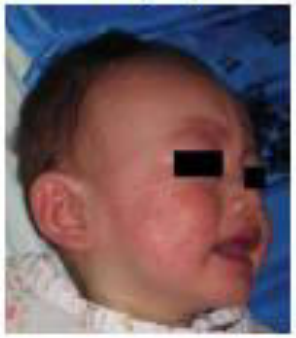

Chikungunya


EV 71

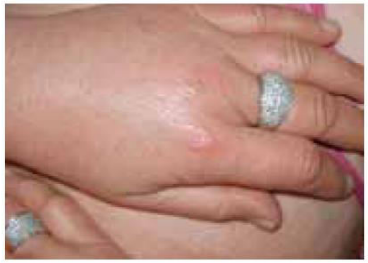

Viral Encephalitis

Manifestations of Chikungunya have an Acute and a Chronic Component

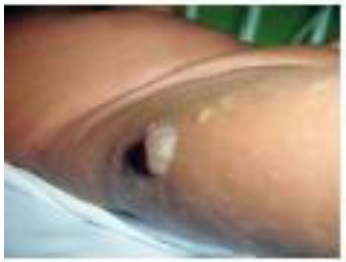
Acute (2-10 days)



Edematous rash

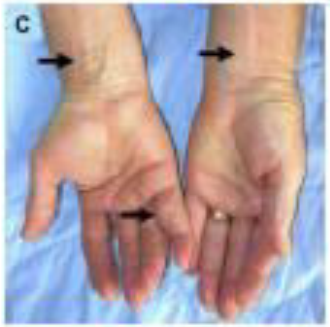


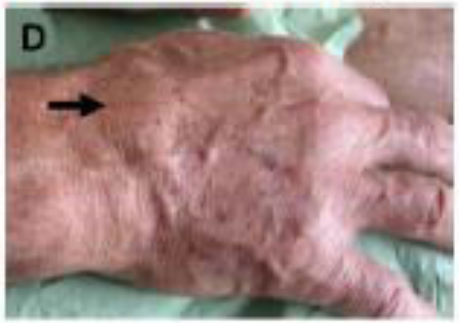
B. Edematous poylarthritis of the hands



Myalgia

Chronic (months to years)





Inflammatory osteoarthritis

Swollen and stiff joints

DIAGNOSIS

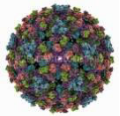
Requires rapid, comprehensive and systematic approach

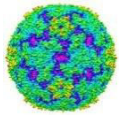
Early ID of cause crucial for management and prognosis

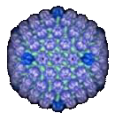
Evaluation of child with altered brain function

- Assessement of airway
- Breathing
- Circulation

Priorities are stabilization of cardio-respiratory status, management of seizures


Chikungunya

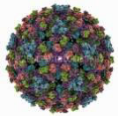

EV 71

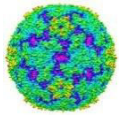

Viral Encephalitis

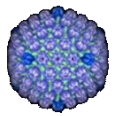
http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

APPROACH TO DIAGNOSIS

History
Symptoms: fever; depressed or altered level of consciousness; lethargy; personality change; emotional lability; seazure; ataxia
Travel
Exposure (animals, insects, freshwater swimming, toxins
Immunizations
Immune status
Physical findings
Vital signs and general examination
Neurologic examination, particularly for focal findings and GCS


Chikungunya


EV 71


Viral Encephalitis

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

APPROACH TO DIAGNOSIS

Laboratory studies

Screening laboratories: CBC; glucose; electrolytes; BUN; creatinine; ammonia; blood pH; blood cultures; LFTs; urinalysis; urine drug screen; save a sample of acute serum

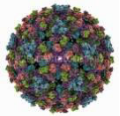
Lumbar puncture; perform emergently, often after neuroimagingif a focal lesion is suspected; obtain opening pressure when clinically feasible; send CSF for cell count/ differential, glucose, protein, bacterial culture, HSV PCR, enterovirus PCR; save a sample PCF

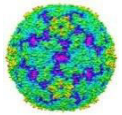
Other laboratory tests to consider: Influenza testing during influenza season; tests for toxic metabolic encephalopathy and inborn errors of metabolism (see text); antibody studies for NMDAR and VGKC (see text)

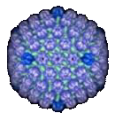
Ancillary studies

Neuroimaging: MRI preferred, but CT if MRI not promptly available, impractical, or cannot be performed

EEG: as soon as is feasible (for evidence of encephalitis or nonconvulsive seizure)


Chikungunya

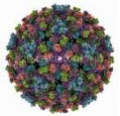

EV 71

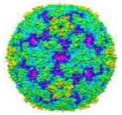

Viral Encephalitis

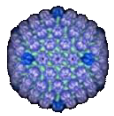
http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

APPROACH TO DIAGNOSIS

Treatment
Stabilization
Support airway, breathing and circulation
Endotracheal intubation for GCS $\leq$ 8 or compromised airway
Fluid resuscitation with normal saline (20 mL/kg, initial bolus) for sings of shock
Obtain rapid glucose; treat if hypoglycemic with 2.5mL/kg of 10% dextrose solution
Treat seazures with lorazepam (0.1 mg/kg intravenously) or equivalent benzodiazepine


Chikungunya


EV 71


Viral Encephalitis

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

APPROACH TO DIAGNOSIS

Treatment

Empiric therapy (initial dose)*
Treat for influenza, as indicated, during influenza season with oseltamivir (0 to 3 months: 12 mg orally; 4 to 5 months: 17 mg orally; 6 to 11 months; 24 mg orally; ≥ 12 months and ≤ 15 kg: 30 mg orally; 15 to 23 kg: 45 mg orally; 23 to 40 kg: 60 mg orally; > 40 kg and/or > 12 years old: 75 mg orally)
Administer acyclovir (> 29 days to < 12 years: 20 mg/kg intravenously; ≥ 12 years: 10 mg/kg intravenously) to all patient without a specific diagnosis other than HSV
Treat for bacterial meningitis as indicated (eg vancomycin [15 mg/kg intravenously] **plus either** ceftriaxone [50 mg/kg intravenously] or cefotaxime [100 mg/kg intravenously)
Treat for rickettsial infection (eg, Rocky Mountain spotted fever, Q fever) or ehrlichiosis in children at risk (doxycycline [2.2 mg/kg intravenously or orally])

http://www.uptodate.com/contents/acute-viral-encephalitis-in-children-and-adolescents-pathogenesis-and-etiology

PREVENTION AND CONTROL

EV 71

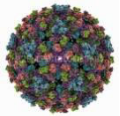
- Vaccine is currently being develop

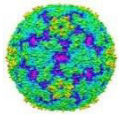
Chikungunya

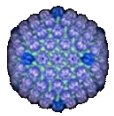
- No vaccine available

Japanese B

- Vaccine available
  - Live-attenuated
  - Inactivated
  - Routinely administered in Thailand, Malaysia


Chikungunya


EV 71


Viral Encephalitis

THANK YOU