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Enterovirus D68

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中區傳染病防治醫療網
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腸病毒D68的發現: I

- 科學家在2012-2014之間發現數十名不明皮疹的孩童與肢體麻痺呈現相關性，並由他們的呼吸道分離出新型腸病毒D68
- 研究發現這型孩童的新型腸病毒D68-B1會造成弛緩性脊髓炎(flaccid myelitis)，通常先前都會先出現呼吸道疾病
- 這些病人的呼吸道分泌物、血中、腦脊髓液中均沒有分離出EV-D68以外足以造成肢體麻痺的病原菌,但也不知究竟如何造成孩童肢體麻痺的

Source: Enterovirus D68 Paralysis - Huffington Post

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腸病毒D68的發現: II

- 此項觀察將EV-D68與兒童突發肢體麻痺或肌肉無力相連結,但沒有明確的將之與弛緩性脊髓炎(flaccid myelitis)做出因果連結，這將是將來EV-D68及疫苗研究的重點
- EV-D68-B1約在四年前出現，就如同EV-D70及小兒麻痺病毒一樣會造成神經損傷或麻痺，其為2014年流行的主要病毒株，但從2014年8月到2015年3月，只有一小部分病人(34州共115人)產生肢體麻痺的後遺症

Source: Enterovirus D68 Paralysis - Huffington Post

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EV-D68

- AKA: Enterovirus-D68
  - 549 cases in 43 states as of Oct 6, 2014
- Children with asthma at higher risk
- No specific treatment / cure
- Question of paralysis side effect

(CDC, 2014)

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What is enterovirus 68

- Enterovirus 68 (EV68, EV-D68, HEV68) is a member of the *Picornaviridae* family, an enterovirus. First isolated in California in 1962 and once considered rare, it has been on a worldwide upswing in the 21st century. With some uncertainty, it has been implicated in cases of a polio-like disorder called acute flaccid myelitis.

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EV68的生物特性

- EV68是100多種腸病毒中的一隻，為單股RNA病毒，無外套膜
- EV68不同於其它腸病毒的特性在於對酸不穩定，並喜歡在低溫生長，這些特性都偏向鼻病毒(rhinovirus)，以前曾將其歸類為人類鼻病毒87型

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EV68流行病學

- EV68自從1962年被發現後，普遍認為只會造成偶發性人類感染
- 從2005-2011共有過6次小規模(>10人)的感染爆發，分別出現在菲律賓、日本、荷蘭、美國喬治亞州、賓州、及亞利桑納州
- 2012-2013之間在加州通報的五名類小兒麻痺幼童中，有兩人分離出EV68EV68，病例經CDC分析都出現在溫暖的月份(春天到秋天)

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EV68好發因子

- 小於五歲的小孩及有氣喘的小孩風險最高
- 氣喘或免疫抑制的成人也偶有感染的報告

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2014年北美EV68感染爆發

- 2014年八月，EV68在美國出現呼吸道感染爆發
- 到10月中已在46個州及哥倫比亞特區出現691個病人，5個孩子死亡

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臨床表現

- EV68感染幾乎都表現出呼吸道感染，由輕到種都有，初始症狀像感冒，包括流鼻涕、喉嚨疼、咳嗽、及發燒
- 疾病進行下去會演變成肺炎、神智不清、尿量減少、缺水、呼吸衰竭
- 和其它腸病毒感染一樣，某些人也會出現皮疹、腹痛、及軟便

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Enterovirus (EV-D68) Symptoms

- **Mild symptoms may include:**
  - Fever
  - Runny nose
  - Sneezing
  - Cough
  - Body and Muscle aches
- **Severe symptoms may include:**
  - Wheezing
  - Difficulty breathing

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急性軟弱型脊髓炎

- 在加州兩名EV68感染的幼童，在感染48小時之後就產生一肢或數肢肢體麻痺，EV68因此被懷疑是元凶，追蹤6個月病酮的肢體麻痺恢復有限
- 2014年10月美國CDC調查國內通報的10例肢體麻痺或腦傷的病童，發現也與EV68的流行正相關，到10月23日通報的病例就達到將近100人
- 發現於1962年的EV68病毒可造成的疾病譜相當廣，從輕微的類流感到嚴重的呼吸窘迫，最近更出現半身或全身麻痺的病例，感染者都有暴露過腸病毒的風險，健康成人感染偏向無症狀
- EV68確與年輕孩童及虛弱孩童的肢體麻痺有相關，然而472位感染者中僅不到100人出現嚴重症狀(包含肢體麻痺)，且僅有一例死亡，此病例是一10歲的新罕布爾州的女孩

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診斷

- 美國CDC研發的real-time PCR試驗可快速診斷此病毒

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治療

- 腸病毒D68目前沒有疫苗與藥物，只需症狀治療
- 大多數病人會完全康復，但某些人必須住院，有些人會死亡
- 五個腸病毒D68的病例曾以類固醇、IVIG、血漿置換成功治療，但並沒有因此恢復神經學的功能
- 一項2015的研究報告證實抗病毒藥物pleconaril對腸病毒D68治療有效

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預防

- 依據美國CDC的建議，預防傳染的方法是不要接觸病童，因為病毒可出現在口水、黏液、糞便。手衛生也是很重要的。病人打噴嚏戴口罩，物面環境及玩具的清潔也是很重要的項目
- 對於EV-D68的住院病人，美國CDC建議除了建議對所有病人執行transmission-based precautions (standard precautions, contact precautions)之外，尚須執行droplet precautions

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環境清潔消毒

- 依據2003年美國CDC的指南建議，若要消毒無外套膜的病毒(例如諾羅病毒、小兒麻痺病毒、鼻病毒)，醫療院所的物體表面必須用EPA核准的醫療級別的消毒劑進行消毒

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Enterovirus D68 Illness in Hospitalized Children under 24 Months of Age

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Introduction

- Enterovirus D68 (EV-D68) is a poorly described cause of acute respiratory tract infection (ARTI), and disease is rarely reported in children <24 months.
- In August 2014, Children's Mercy Hospital (CMH) reported an increase in severe ARTI associated with EV-D68.
- We sought to characterize EV-D68 disease in young children by comparing hospitalized children with EV-D68 with hospitalized children with other enteroviruses/rhinoviruses.

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Methods

- Retrospective chart review was conducted on hospitalized children <24 months with positive multiplex-PCR testing for enterovirus/rhinovirus at Children's Mercy Hospital from 8/1-9/15/14.
- Patient specimens were tested to confirm EV-D68 by sequencing and/or real-time PCR.
- Demographics, underlying conditions, clinical features, laboratory results, therapeutics, and outcomes of hospitalized EV-D68 infected children were compared with hospitalized children infected with other enteroviruses/rhinoviruses

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Results

- 187 enterovirus/rhinovirus positive specimens were collected from hospitalized children <24 months.
  - 80 (42.8%) were EV-D68 positive
  - 102 (54.5%) were EV-D68 negative
  - 5 (2.7%) specimens were unable to be typed

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	EV-D68 positive n=80 (%)	EV-D68 negative n=102 (%)	P value
Median age- months (IQR)	13.0 (9.0-19.0)	8.5 (2.0-16.0)	0.001
Past medical history of asthma or reactive airway disease	24 (30.0)	20 (19.6)	0.1

Table 1. Baseline characteristics of hospitalized children with EV-D68 and hospitalized children with other enteroviruses/rhinoviruses.

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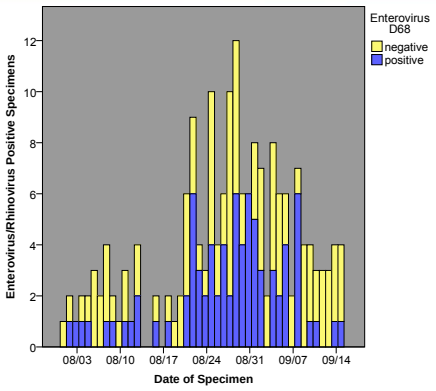

Figure 1. Entero/rhinovirus positive specimens in hospitalized children <24 months of age.

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Symptoms	EV-D68 positive n=80 (%)	EV-D68 negative n=102 (%)	P value
Cough	67 (83.8)	65 (63.7)	0.003
Nasal congestion	43 (53.8)	39 (38.2)	0.04
Rhinorrhea	39 (48.8)	34 (33.3)	0.04

Table 2. Symptoms of children admitted with EV-D68 compared to children admitted with other enteroviruses/rhinoviruses

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Physical findings	EV-D68 positive n=80 (%)	EV-D68 negative n=102 (%)	P value
Retractions	56 (70.0)	43 (42.2)	<0.001
Wheezing	42 (52.5)	29 (28.4)	<0.001
Tmax ≥38.5°C	15 (18.8)	19 (19.0)	0.97

Table 3. Physical findings of children admitted with EV-D68 compared to children admitted with other enteroviruses/rhinoviruses

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Therapies	EV-D68 positive n=80 (%)	EV-D68 negative n=102 (%)	P value
Intensive care management	12 (15.0)	16 (16.0)	0.85
Oxygen	58 (72.5)	45 (45.0)[1]	<0.001
Albuterol	62 (77.5)	44 (44.0)[1]	<0.001
Corticosteroids	48 (60.0)	34 (34.0)[1]	0.001

Table 4. Therapies received by children admitted with EV-D68 compared to children admitted with other entero/rhinoviruses.[1] n=100

Outcome	EV-D68 positive n=80 (%)	EV-D68 negative n=102 (%)	P value
Discharged with albuterol	57 (71.3)	33 (32.4)	<0.001
Discharged with corticosteroids	32 (40.0)	20 (19.6)	0.003
Median length of stay-hours (IQR)	38 (19.0-67.0)	36 (21.3-72.5)[1]	0.85

Table 5. Outcome of children admitted with EV-D68 compared to children admitted with other entero/rhinoviruses.[1] n=100

Conclusion

- EV-D68 positive children <24 months of age were
  - Older
  - More likely to have respiratory symptoms
  - More likely to have wheezing and increased work of breathing on physical exam
  - More likely to receive asthma-directed therapies, despite no difference in past medical history between the two groups
- EV-D68 positive children were not more likely to require intensive care unit management or have longer length of stay

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The Rehabilitation Implications of Children Diagnosed with Enterovirus D68: A Case Study

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Introduction

- Outbreak of Enterovirus D-68 between August 2014 and January 2015 spanning 49 states in the United States
- 1153 cases confirmed by the Centers for Disease Control
- Approximately two-thirds of all known cases reported various levels of recovery

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Background

- EV-D68 is a member of the Picornaviridae family, an enterovirus which has been associated with acute flaccid myelitis, a polio-like illness
- CDC Case Diagnosis Criteria for AFM:
  - 21 years or less
  - Acute onset of limb weakness
  - Onset on or after August 1, 2014
  - MRI lesions in spinal gray matter
- Most vulnerable patients:
  - Less than 21 years
  - Asthma or other respiratory illness
  - Other comorbidities
- Symptoms:
  - Fever

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History

- 6 year old female with history of 27 week gestation, asthma, and bronchpulmonary dysplasia. Admitted to hospital after three outpatient clinic visits for worsening respiratory symptoms accompanied by decreased head control and overall weakness on day of admission

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Clinical Examination

- On initial Rehabilitation consult, patient scores for strength were all less than 3/5, with distal weaker than proximal areas. She was ventilated via tracheostomy and required total care for all activities of daily living. Her face was symmetrical. All extra ocular movements were intact. Neuropathic pain was present globally and difficult to control.

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Diagnosis and Management

- EV-D68 was entered into the differential by neurology at the time Rehab was consulted. Management was handled by various specialties including pulmonology, neurology, infectious disease, palliative care, and rehabilitation medicine. Some techniques used in managing this patient included:
  - Gastrostomy
  - Tracheotomy
  - Mechanical ventilation
  - Pharmacologic pain management
  - Rehabilitation
  - Physical therapy
  - Occupational therapy
  - Speech therapy
  - Sunshine School
  - Family Education and training

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Outcome

- The patient currently attends physical, occupational , and speech therapies on an outpatient basis. She continues to require ventilation via tracheostomy. Currently her therapists estimate an approximate 20% return of sensation to her left side with strength of 2/5 to her left lower extremity, only when removing gravity. Her left upper extremity has strength rating of 1/5 to the wrist and hand only. She has had a 90% return of sensation and function of her right lower extremity. Current therapy goals include the exploration of technology to increase her independence with school and operating a custom wheelchair with an adaptive control.

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Summary

- Prognositcation for EV-D68 continues to be limited
- Questions have been raised as to possible future implications of Acute Flaccid Myelitis as it compares to Post Polio Syndrome
- CDC will continue to study EV-D68 and monitor possible future outbreaks

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