



上呼吸道感染之鑑別診斷與處置 Treatment of Upper Respiratory Tract Infection in Children

主講人:邱政洵醫師 長庚紀念醫院 兒童內科部







課程大綱

- 1. Common Cold
- 2. Pharyngitis
- 3. Influenza
- Croup, Epiglottitis, Laryngitis, and Bacterial Tracheitis
- 5. Deep Neck Infections in Taiwan
- 6. Otitis Media
- 7. Sinusitis







1. Common Cold







Common Cold

- Acute, communicable, viral disease.
- Characterized by nasal stuffiness, sneezing, coryza, throat irritation, no or minimal fever.







Epidemiology

- More than 100 serologically different viruses.
- Average number of colds: 3~8/child/year.
- Initial focus in the school.
- Secondary attack rate: adult=1/2 children.
- Close personal contact necessary for transmission.
- Greatest concentration of virus in the nasal secretions: sneezing, nose blowing, contamination with nasal secretions.







Frequency of Respiratory Illnesses by Age

Age	Respiratory illnesses episodes per child-year		
(years)	Cleveland, 1970s	Linko, 1990s	
<1	6.7	6.9	
1	8.3	8.9	
2	8.1	10.5	
3	7.8	8.5	
4	7.6	8.3	
5	7.4	5.2	







Treatment

- No clinically available antiviral agents.
 - No specific therapy in the majority except RSV and influenza.
- Specific symptomatic care.
 - Analgesic.
 - Relief of nasal obstruction.
- Antibiotics: no place.
- Vitamin C: controversial.







2. Pharyngitis







Pharyngitis(Tonsillitis, Tonsillopharyngitis, Nasopharyngitis)

- An inflammatory illness of mucous membranes and underlying structures of throat.
 - Frequently involve nasopharynx, uvula, tonsil, soft palate.
 - Erythema, exudate, ulceration.
 - Usually acute, throat discomfort or not.





Common Causes of Pharyngotonsillitis

- Group A beta-hemolytic streptococci.
- Adenovirus.
- Influenza viruses.
- Enteroviruses.
- Parainfluenza viruses.
- Epstein-Barr virus.
- New viruses(hMPV, hBoV, and hCoV NL63 and HKU1).







Etiology of Acute Pharyngitis in Children

- During May 1999 and April 2000, MMH, Taipei.
- 416 children, 53 + 37 m/o, with acute pharyngitis at OPD.
- Virus detected in 123 cases(29.6%).
- Bacteria isolated in 73(17.5%) cases.

- Group A Streptococcus in only 7 cases(1.7%).

• Both bacteria and virus in 46 cases(11%).







Potential Pathogens Isolated from 416 Patients with Acute Pharyngitis

Microorganism	No. of isolates (%)
Bacteria	122 (29.3)
Haemophilus influenzae non-type b	41 (9.9)
Haemophilus parainfluenzae	40 (9.6)
Haemophilus influenzae type b	15 (3.6)
Staphylococcus aureus	14 (3.4)
Group A Streptococcus	7 (1.7)
Streptococcus pneumoniae	4 (1.0)
Serratia marcescens	1 (0.2)
Virus	175 (42.1)
Adenovirus	110 (26.4)
Herpes simplex virus type 1	43 (10.3)
Coxsackievirus	10 (2.4)
Parainfluenza virus	4 (1.0)
Influenza virus	3 (0.7)
Respiratory syncytial virus	3 (0.7)
Cytomegalovirus	2 (0.5)

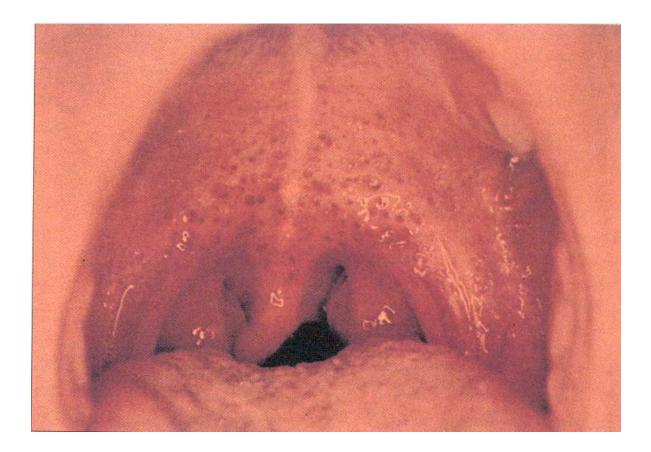
資料來源: Chi H et al J Microbiol Immunol Infect 2003; 36:26-30







GAS Pharyngotonsillitis









Methods

- In January 2009-December 2010, up to 5 cases of children with initial diagnosis of respiratory tract infection in Chang Gung Children's Hospital per week were randomly selected for viral etiology investigation after a written consent was obtained.
- Throat swabs were obtained from each case and sent for viral detection by virus isolation and polymerase chain reaction(PCR).







Results(1/2)

- Detection of respiratory viruses.
 - During January 2009 to December 2010, total 360 cases were recruited and laboratory tests were completed in 360 cases.
 - Viral etiology was identified in 257(71.4%) cases with total 314 viruses identified.
 - 34.7%(109/314) identified viruses were through PCR.
 - Mixed pathogens were found in 49(13.6%) cases.







Results(2/2)

Virus detection	Case No. (%)
Cases enrolled	360
By virus isolation	
Influenza A virus	17 (5)
Influenza B virus	7 (2)
Parainfluenza virus	
1	11 (4)
2	8 (3)
3	12 (4)
RSV	14 (4)
Adenovirus	50 (16)
Enterovirus	70 (22)
Cytomegalovirus	9 (3)
Herpes simplex virus	7 (2)

By PCR	Case No. (%)	
CoV-OC43	4	
CoV-229E	0	
CoV-NL63	1	
Bocavirus	24 (8)	
hMPV	79 (25)	
CPE	1	
Mixed	49 (18.9)	
Negative	103 (28.6)	

Five most common identified viruses:

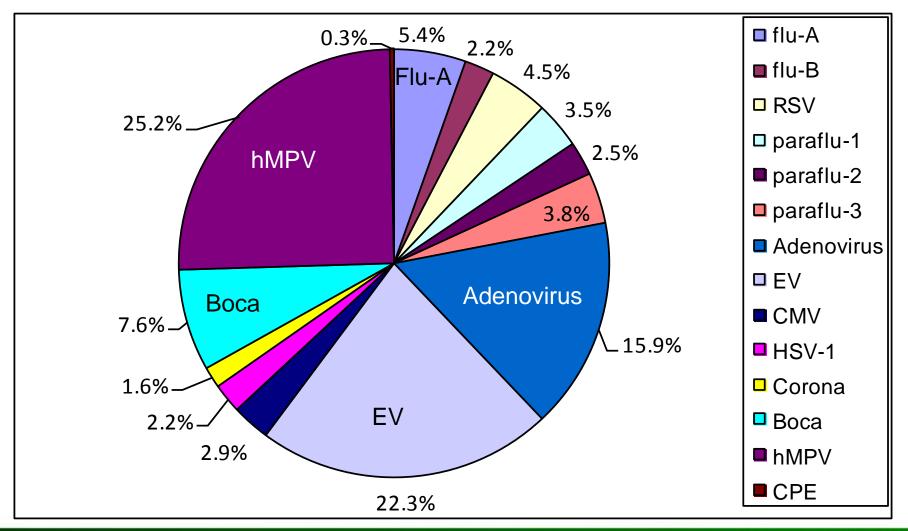
Taiwan CDC http://www.cdc.gov.tw

- hMPV
- Enterovirus
- Adenovirus
- Bocavirus
- Influenzae A





Distribution of Identified Virus



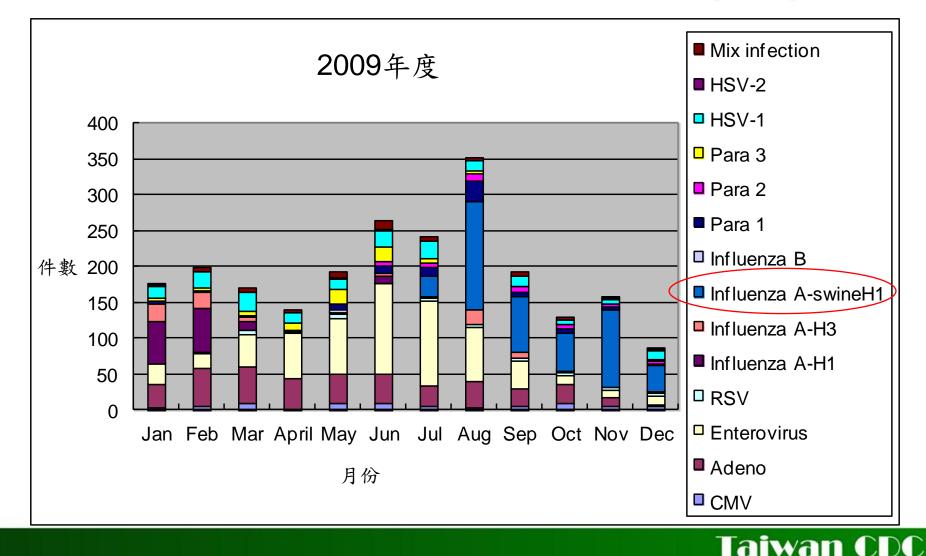






http://www.cdc.gov.tw

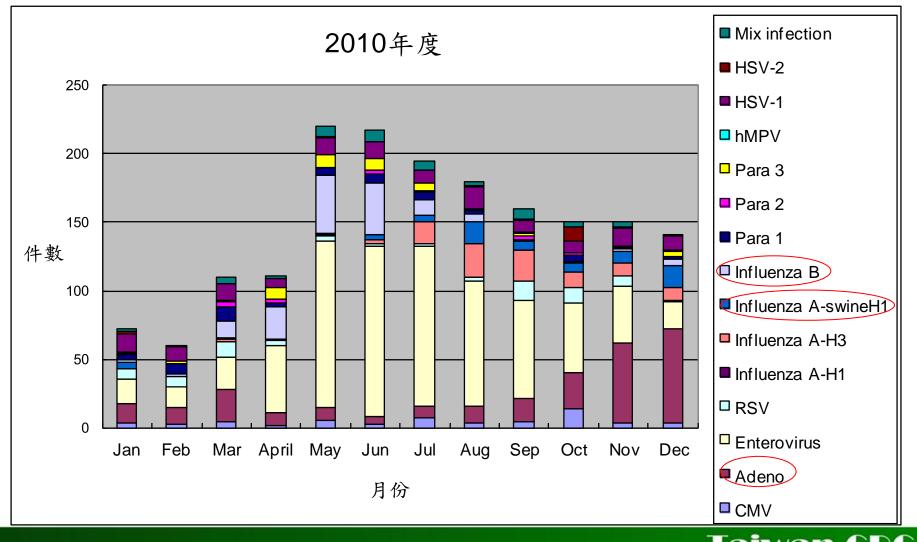
林口長庚醫院病毒培養結果(1/2)







林口長庚醫院病毒培養結果(2/2)



Taiwan CDC http://www.cdc.gov.tw





Demographic characteristics and clinical presentations in children with virus negative or virus positive.

衛生福利部疾病管制署

- Male gender(p=0.04) and relatively young age (p=0.003) were significantly more common among children with multiple respiratory viral infection.
- There were no significant differences when comparing the group of no virus with single or multiple virus infection in antibiotic use, diagnosis of LRTIs, nor length of hospitalization.







Diagnosis of Pharyngitis

- Diagnosis of GAS pharyngitis based on results of appropriate laboratory tests with clinical and epidemiologic findings.
 - Throat culture, rapid antigen test to confirm.
 - Age, odynophagia, fever, reactive neck
 lymphadenopathy, abdominal pain, and absence of viral syndrome.
- Viral isolation and identification.







http://www.cdc.gov.tw

Principles of Judicious Use of Antimicrobial Agents for Pharyngitis

- Clinical findings neither sensitive nor specific for GAS pharyngitis, Dx based on a laboratory test.
 - Throat culture-the standard for diagnosis.
- Viral agents cause most pharyngitis episodes.
- Bacteria other than GAS rare causes of pharyngitis.
 - Group G and C Streptococcus, N. gonorrhea, Arcanobacterium haemolyticum, C. diphtheriae.







IDSA Guidelines for Diagnosis and Management of Group A Streptococcal Pharyngitis

- Therapy
 - Antibiotics: penicillin and its congeners, 1° generation cephalosporins, macrolides(not in Taiwan), clindamycin.
 - Duration: 10 days.
 - A small percentage has a recurrence.









3. Influenza







Influenza Virus

Type A (16 HA and 9 NA subtypes)

- Found mainly in birds, swine, human.
- H1, H2, and H3 subtypes adapted to human.
- Seasonal epidemics or pandemics; mild to severe illness.
- H5, H6, H7, H9, and H10 subtypes, sporadic infection.

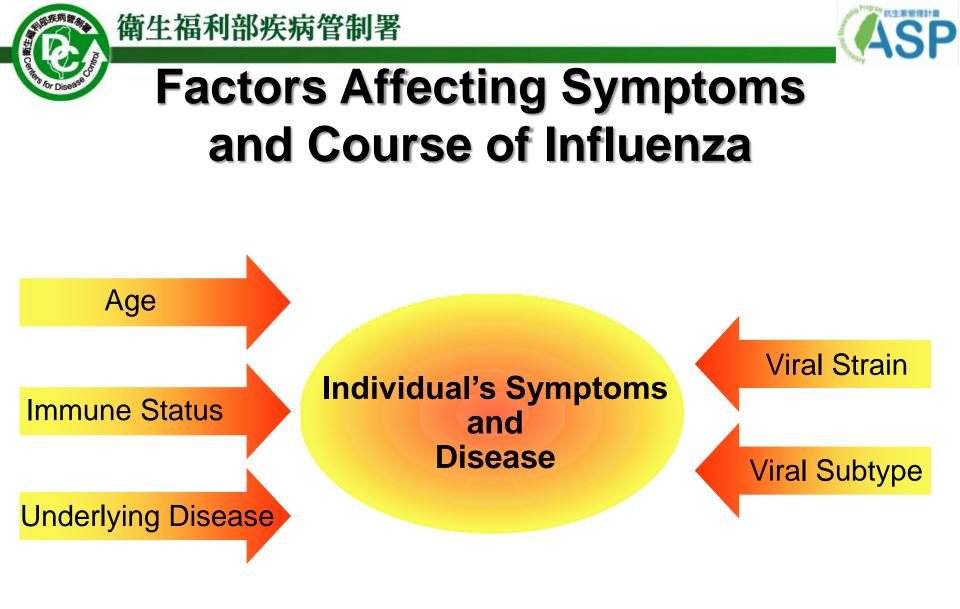
Type B (Victoria and Yamagata lineage)

- Found only in human; causing seasonal epidemics.
- Mild to severe illness.

Туре С

Found in mammals; causing mainly mild illness.









Signs and Symptoms

- Abrupt onset of symptoms.
- Fever, usually over 100°F.
- Nonproductive cough.

衛生福利部疾病管制署

- Chills and/or sweating.
- Headache.
- Myalgia.
- Sore throat.

- Potentially severe, persistent malaise.
- Substernal soreness, photophobia, and ocular problems.

ILI:

fever, respiratory symptoms, systemic symptoms

aiwan

http://www.cdc.gov.tw





Recognizing Pediatric Influenza

Neonates	Infants/Toddlers	Children/Teens
High fever	GI symptoms	Rapid onset
Lethargy	Fever > 103°F (>39.5°C)	High fever
Decreased eating	Anorexia	Cough
Mottling	Respiratory syndromes	Chills
Apnea	Malaise Irritability	Malaise Headache Sore throat











Influenza A vs. B in Children

	2001-2006, NCKU, Taiwan	
type	Influenza A	Influenza B
Total case numbers	163	118
Mean age, years	5.7	6.7
Hospitalization	36%	40%
Upper respiratory disease	45%	64%*
Lower respiratory disease	28%	26%
Myositis	2%	14%*
Gastroenteritis	3%	22%*
Invasive disease	3%	6%

* P < 0.05







Children Were the Major Target Population in Household Influenza Transmission

	Number	Mean age, years	Positive tested(%)
Index case	87	11	87/87 (100)
Household members	223	34	60/223 (27)
Children	57	8	35/57 (61) *
siblings	56	8	35/56 (63)
cousin	1	12	0/1 (0)
Adults	166	43	25/166 (15) *
siblings	5	20	0/5 (0)
parents and others	138	41	25/161 (16)

* P <0.01







Guidelines for Antiviral Therapy of Acute Upper Respiratory Tract Infection in Taiwan

- For influenza
 - During epidemic period, antiviral agents given in highrisk groups(chronic obstructive airway disease, cardiovascular disease, immunocompromized host, health care workers, the elderly) in first 24-48 hrs.
 - Drug of choice: amantadine(influenza A only), rimantadine(influenza A only), oseltamivir, zanamivir(inhalation).







4. Croup, Epiglottitis, Laryngitis, and Bacterial Tracheitis





Croup Syndrome

• One of more common childhood respiratory illnesses.

衛生福利部疾病管制署

- A group of inflammatory diseases involving airway, characterized by barking cough, hoarseness and inspiratory stridor.
- Include viral laryngotracheobronchitis, spasmodic croup, bacterial tracheitis and epiglottitis.







Viral Croup

• Highest attack rate in second year of life.

- 4.7~6/100 children year.

- Male predominant(2:1).
- Seasonal peak in late autumn and winter.
 Throughout the year in Taiwan.
- Common etiology: parainfluenza virus type I, II, III, RSV, influenza virus, *M. pneumoniae*.







http://www.cdc.gov.tw

Childhood Croup Syndrome in Northern Taiwan

- April 1990~January 1996, NTUH, Taipei.
- 132 children, aged 3 months to 7 years.
 - Laryngotracheitis(croup) in 123 cases(93.2%): 23 pathogens identified(parainfluenza 7, RSV 5, influenza A 4, *M. pneumoniae* 4, adenovirus 3).
 - Bacterial tracheitis in 7: viridans streptococci 6,
 S. aureus 1.
 - Spasmodic croup 1.
- High fever > 3 days, more likely bacterial tracheitis or bacterial complications.





http://www.cdc.gov.tw

Management of Viral Croup

- Steroids: mechanism not definitely known.
 - Both systemic or inhaled form reduce morbidity and hospitalized time.
 - A single dose of oral or IM 0.15~0.6 mg/kg dexamethasone.
 - Nebulized 2 mg budesonide.
- Epinephrine: effect last only a few hours.
 - Nebulized a dose of 0.1 ml/kg of 1% solution or 4 ml of 1:1000 preparation.
- Mist therapy: little evidence for any beneficial effect.

資料來源: Geelhoed GC Pediatr Pulmonol 1997; 23:370-4





Epiglottitis(1/2)

- Inflammation and edema of epiglottis.
- Usually caused by *H. influenzae* type b.
- Characterized by rapid onset and progression
 - Death may occur due to obstruction of airway.
 - An ENT emergency.
- Treatment: airway established and appropriate antibiotic.





衛生福利部疾病管制署



Epiglottitis(2/2)

• Causes

Children

- Haemophilus influenzae type b
- Diphtheria
- Staphylococcus aureus
- Streptococcus pneumoniae
- Group A Streptococcus

Adults

- Same as children
- Nontypeable Haemophilus spp.



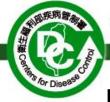




Clinical Features of Acute Epiglottitis

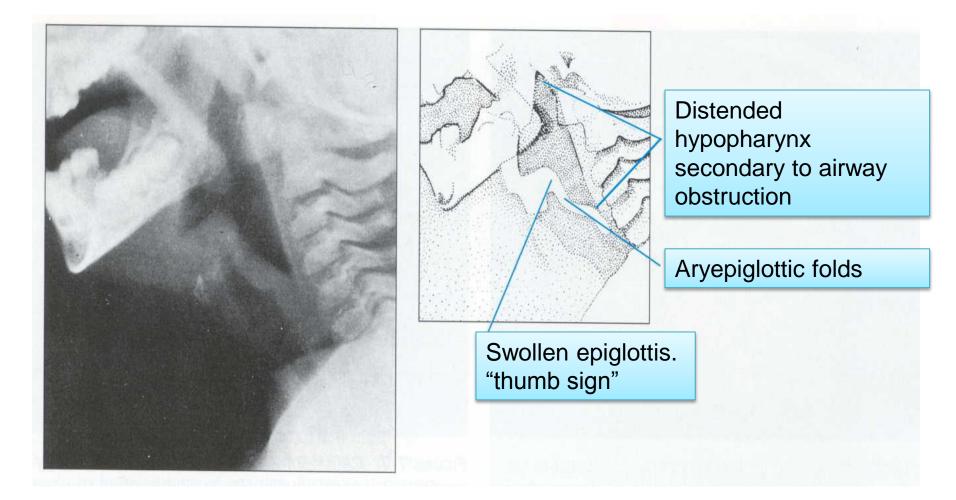
	Children	Adults
Age at acquisition	3-5 years	_
Location of pathology	Supraglottic	Supraglottic
Onset	Rapid	Most have a mild illness with prolonged course, painful dysphagia, and pharyngitis
Fever	High	Variable
Appearance	Toxic	Usually not toxic
Stridor	+++	Not usual
Cough	Not usual	-
Drooling	Often	-







Lateral Neck X Ray(hyper-extension)









Guidelines for Antimicrobial Therapy of Acute Upper Respiratory Tract Infection in Taiwan

- For acute epiglottitis.
 - Drug of choice: amoxicillin/clavulanate, ampicillin/sulbactam, 2° or 3° cephalosporins.
 - Alternatives: chloramphenicol, aztreonam, imipenem or meropenem.
 - Antimicrobial therapy should be intravenous administration.







5. Deep Neck Infections in Taiwan







Etiology of Deep Neck Infections

Table 2. Etiology of deep neck infections.

Etiology	No. patients (%) (<i>N</i> = 185)
Odontogenic	42 (22.7)
Upper airway infection	24 (13)
Peritonsillar abscess	7 (3.8)
Foreign body (digestive tract)	2 (1.1)
Surgery of aerodigestive tract	2 (1.1)
Skin infection	1 (0.5)
Parotitis	1 (0.5)
Unknown	106 (57.3)





Antecedent Illness and Site of Deep Neck Infection in 68 Children

Table 2. Antecedent illness and site of deep neck infection in 68 children

	Total	Peritonsillar	Retropharyngeal	Parapharyngeal	Submandibular
	n=68, (%)	n=14, (%)	n=25, (%)	n=21, (%)	n=8, (%)
Tonsillitis	2 (2.9)	1 (14.3)	1 (4)	0	0
Viral URI	11 (16.2)	3 (21.4)	4 (16)	4 (19.1)	0
Sinusitis	4 (5.9)	1 (14.3)	2 (8)	1 (4.8)	0
Dental infection	2 (2.9)	0	0	0	2 (25)
Trauma	7 (10.3)	0	6 (24)	1 (4.8)	0
Congenital cyst	5 (7.4)	0	0	4 (19)	1 (12.5)
Unknown	37 (54.4)	9 (64.3)	12 (48)	11 (52.4)	5 (62.5)



資料來源:Tan PT, et al. J Microbiol Immunol Infect 2001; 34(4):287-92



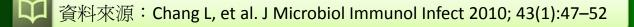




http://www.cdc.gov.tw

Deep Neck Infections

- Sites: 9 in the retropharyngeal space,17 in the parapharyngeal, 21 in the peritonsillar and three with mixed type abscesses.
- S/S: Most retropharyngeal and parapharyngeal abscesses were associated with fever(100% and 65%, respectively) and neck masses(67% and 94%, respectively); while odynophagia was the most common symptom in peritonsillar abscess (100%).







Most Frequent Organisms in Pus Culture

Table 4. Most frequent organisms in pus culture.

Organism	No. patients (%)*
Streptococcus viridans	38 (33.9)
Klebsiella pneumoniae	38 (33.9)
Peptostreptococcus	19 (17.0)
β-hemolytic streptococci	10 (8.9)
Neisseria species	10 (8.9)
Staphylococcus aureus	9 (8.0)
Unidentified anaerobic bacteria	9 (8.0)
Candida	5 (4.5)
Coagulase-negative staphylococcus	4 (3.6)
Enterococcus	4 (3.6)
Eikenella	4 (3.6)

*Of 112 patients with positive cultures, the sum of total percentage exceeds 100 because of mixed infections.









aiwan

http://www.cdc.gov.tw

Microbiologic Isolates in 41 Children with Deep Neck Infection(1/2)

Table 4. Microbiologic isolates in 41 Children with Deep Neck Infection

	Total	Peritonsillar	Retropharyngea	al Parapharyngeal	Submandibular
	N=41	N=10	N=7	N=18	N=6
No growth	2	0	0	1	1
Aerobic					
Viridans streptococci	16	3	8	4	1
GAS	1	1	0	0	0
GBS	3	0	1	2	0
S. aureus	10	0	2	5	3
S. epidermitis	1	0	0	0	1
K. Oxytoca	3	3	0	0	0
K. pneumonia	4	0	3	1	0
Ps. aeroginosa	2	1	1	0	0



資料來源:Tan PT, et al. J Microbiol Immunol Infect 2001 Dec; 34:287-92





Microbiologic Isolates in 41 Children with Deep Neck Infection(2/2)

Table 4. Microbiologic isolates in 41 Children with Deep Neck Infection

Total	Peritonsillar	Retropharyngeal	Parapharyngeal	Submandibular
N=41	N=10	N=7	N=18	N=6
1	0	0	1	0
4	0	1	3	0
1	0	0	1	0
1	1	0	0	0
5 4	1	2	1	0
5	1	2	2	0
18	3	7	6	2
	N=41 1 4 1 1 5	N=41 N=10 1 0 4 0 1 0 1 1 5 1	N=41 N=10 N=7 1 0 0 4 0 1 1 0 0 1 1 0 5 1 2	N=41 N=10 N=7 N=18 1 0 0 1 4 0 1 3 1 0 0 1 1 1 0 0 1 1 0 0 5 1 2 1

GAS= group A streptococcus, GBS =group B streptococcus, Ps=Pseudomonas



資料來源:Tan PT, et al. J Microbiol Immunol Infect 2001 Dec; 34:287-92







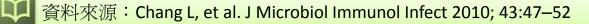
Taiwan

http://www.cdc.gov.tw

Pus Cultures of Patients with Deep Neck Infection Abscess Cavity

Table 3. Pus cultures of patients with deep neck infection abscess cavity (n=32)

Microorganisms	No. of cases
Mixed flora ^a	7
No growth	6
Streptococcus pyogenes	5
Normal flora	5
Streptococcus other than pyogenes	4
Anaerobic bacteria ^b	2
Staphylococcus aureus	1
Klebsiella pneumoniae	1
Bartonella henselae	1







Treatment

- Antibiotics: Amoxicillin ± clavulanate for oral flora, oxacillin or vancomycin for *S. aureus*, 2 or 3rd generation for resistant GNB.
- Drainage for abscess.







6. Otitis Media







Acute Otitis Media in Children

• An extremely common illness in children.

- Almost every child develop one or more episodes.

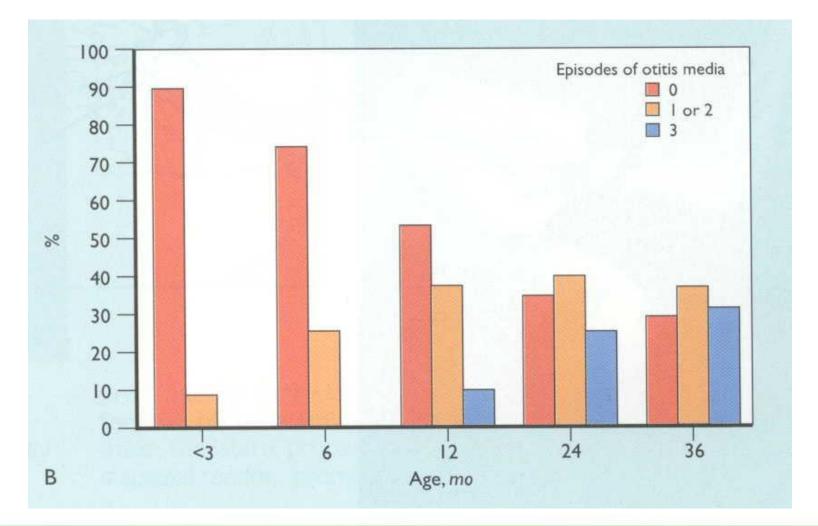
- Peak incidence 6~18 months.
- Otitis-prone children.
- Risk factors.







Episodes of Otitis Media



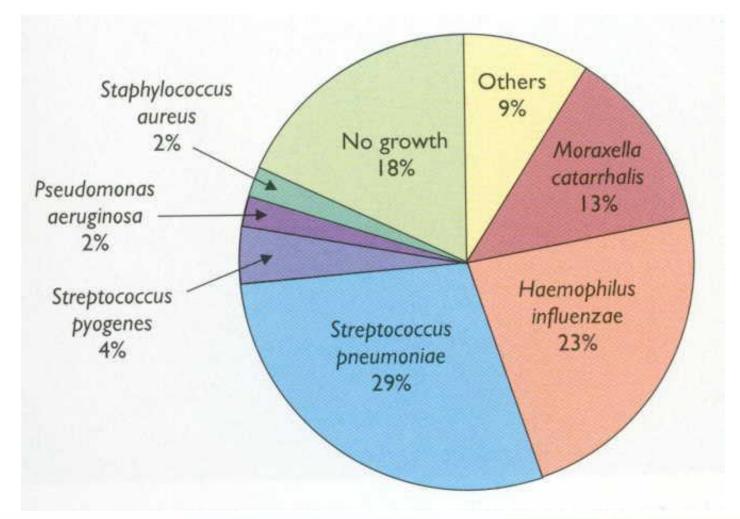








Etiology for AOM









Causative Pathogens of Persistent Otitis Media(1/2)

- September 1997~August 1999, 326. myringotomies and 441 ear fluid specimens from 243 children with severe AOM or unsatisfactory response to antimicrobial therapy.
 - 3 month~14.4 years, mean 3y3m, median 2y7m.
 - Male 58%, 40% < 2 yrs, 71% < 4 yrs.</p>







Causative Pathogens of Persistent Otitis Media(2/2)

- 25 patients(10%) at least 2 episodes during 2year study.
- Complications in 34 patients(14%)
 - Recurrent OM: 22
 - Persistent effusion with tube insertion: 9
 - Hearing impairment: 4
 - CNS infection: 4
 - Mastoiditis: 3
 - Others: 3







Pathogens Isolated from 441 Middle Ear Fluids in 243 Children

Microorganism	No. of isolates(%)
Coagulase-negative staphylococci	146 (33.1)
Streptococcus pneumoniae	96 (21.7)
Haemophilus influenzae	45 (10.2)
Staphylococcus aureus	31 (7.0)
Fungi	9 (2.0)
Pseudomonas aeruoginosa	8 (1.8)
Streptococcus spp.	7 (1.6)
Moraxella catarrhalis	3 (0.7)
Others	30 (6.8)
No growth	66 (15.0)



資料來源:Li WC et al J Microbiol Immunol Infect 2001; 34:190-4







Acute Otitis Media – Clinical Manifestation

Nonspecific

- Fever, irritability, headache, apathy anorexia, vomiting.
- Signs of respiratory viral infection precede.

Specific

 Otalgia, otorrhea, hearing loss, vertigo, tinnitus, swelling about ear, facial paralysis, craniofacial anomalies.







Acute Otitis Media— Complications and Sequelae

- Intracranial: relatively uncommon today
 - Meningitis, extradural abscess, subdural empyema, focal encephalitis, brain abscess, lateral sinus thrombosis.
- Entratemporal
 - Suppurative: perforation of tympanic membrane, cholesteatoma, adhesive otitis media, tympanosclerosis, petrositis, masoiditis, labyrinthitis, facial paralysis.
 - Hearing loss, effects on development of child.







Acute Otitis Media – Management

- Appropriate antimicrobial agent
 - Cover S. pneumoniae and H. influenzae.
 - Amoxicillin or amoxicillin + clavulanate(high dose): the current drug of choice.
 - Resolution of symptoms and signs within 72 hours.
- Symptomatic therapy







Principles of Judicious Use of Antimicrobial Agents for AOM

- Episodes of OM classified as AOM or OME.
- Antimicrobials indicated for treatment of AOM.
 - Diagnosis require documented middle ear effusion and signs or symptoms of acute illness.
- Children < 2 yrs treated with a 10-day course; children > 2 yrs may with a 5 to 7-day course.
- Persistence of middle ear effusion after therapy for AOM is expected and not require therapy.
- Immunization.





Guidelines for Antimicrobial Therapy of Acute Upper Respiratory Tract Infection in Taiwan

- For acute otitis media.
 - Drug of choice: amoxicillin, ampicillin
 - Amoxicillin high dose 80-90 mg/kg/day in 2 divided dose in children.
 - Alternatives: amoxicillin/clavulanate, ampicillin/sulbactam, 2° or 3° cephalosporins(PO).









7. Sinusitis







Sinusitis in Children

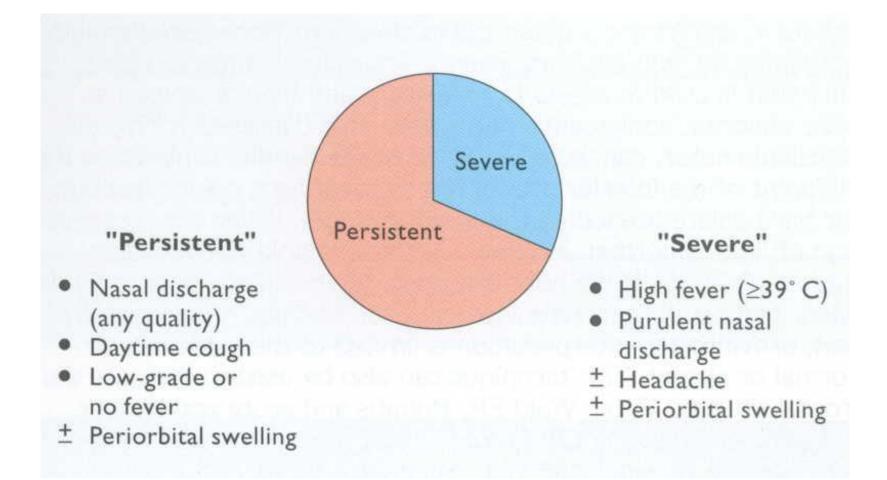
- A common site of infection.
- Frequent morbidity, rare life-threatening complications.
- Predisposing events.
 - Acute viral URTI: 5~13% complicated by a secondary rhinosinusitis.
 - Allergic inflammation.
- Microbiology similar to AOM.
- Acute, subacute, chronic, recurrent acute types.







Persistent & Severe











Sinusitis Complicated by Orbital Cellulitis



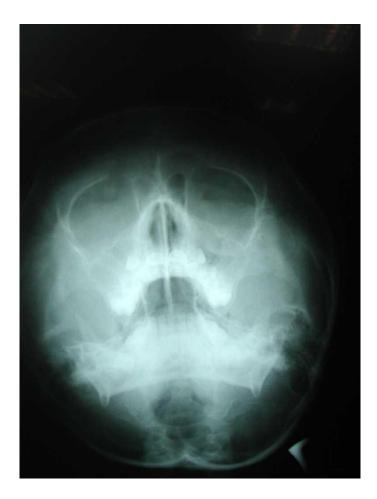








Water's View







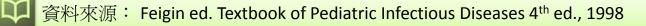


Taiwan

http://www.cdc.gov.tw

Etiologic Agents in Sinusitis in Children

Pathogens	Overall	Acute	Subacute	Chronic
Aerobic bacteria				
H. influenzae	++++	++++	++++	++++
S. pneumoniae	++++	++++	++++	++++
M. catarrhalis	+++	+++	++	+
S. aureus	++	+	+	++
S. pyogenes	++	++	++	++
Anaerobic bacteria				
Peptococcus	++	+	+	++
Peptostreptococcus	++	+	+	++
Mixed	++	+	+	++





Principles of Judicious Use of Antimicrobial Agents for Acute Sinusitis

- Clinical diagnosis requires prolonged nonspecific(e.g., rhinosinusitis and cough > 10~14 days) or more severe(e.g., fever, facial swelling, pain) URTI signs and symptoms.
- Radiographs used and interpreted with caution, indicated when recurrent episodes, suspected complications or unclear diagnosis.
- Initial antibiotic with most narrow-spectrum agent active against the likely pathogens, unless in high risk patients.







Antibiotic Prescribingthe Facts(1/2)

- Prescribing antibiotics in the absence of bacterial infection:
 - Selects for resistance in bacterial flora (and).
 - Has no clinical benefit.
 - Causes unnecessary adverse reactions.
- Prescribing antibiotics to which an organism is resistant:
 - Has no clinical benefit.









Antibiotic Prescribingthe Facts(2/2)

- We must reduce inappropriate antibiotic prescribing.
- This will require:
 - Behavioural change.
 - Education of both physicians and patients.
 - Physician time and resources.
 - An understanding of the impact on resistance.





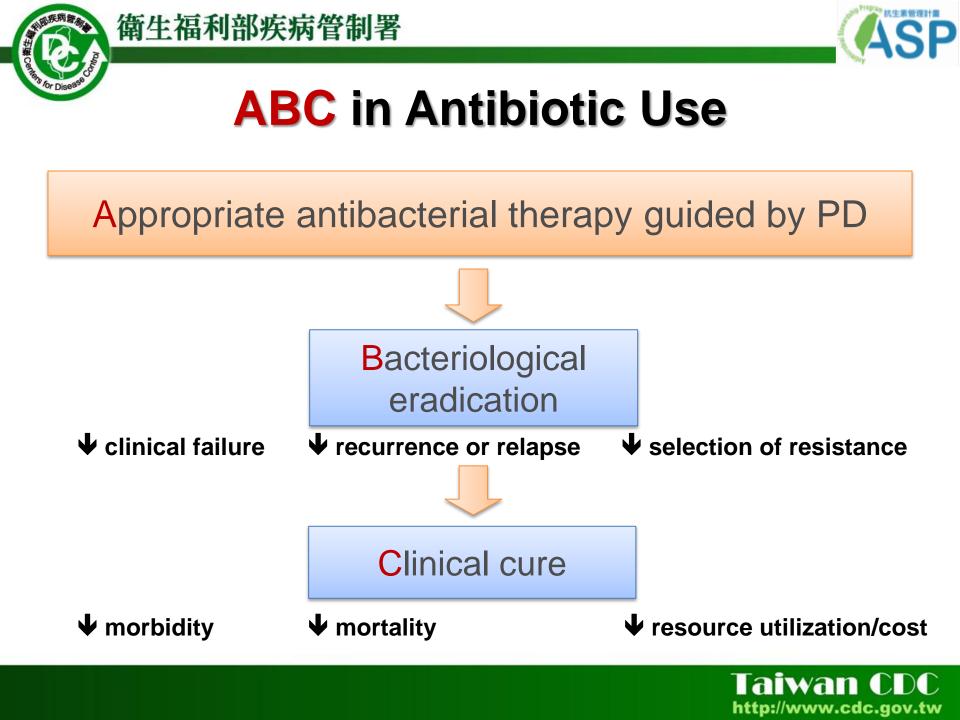




The Need for Change: Investigations by Spanish Primary Care, ID and Chest Societies

"In almost one half of croup, influenza, common cold and in most non-specified ARIs an antibiotic was prescribed." This use of antibiotics is an example of widespread bad practice with no scientific basis whatsoever, which:
"has high economic costs" and "leads to development of resistance"







衛生福利部疾病管制署



Principles Required for Appropriate Prescribing and Effective(Locally Compliant) Guidelines

TREAT	 Bacterial infection only
OPTIMIZE	 Diagnosis/severity assessment
MAXIMIZE	 Bacterial eradication
RECOGNIZE	(Local) resistance prevalence
UTILIZE	 Pharmacodynamics for effective agents and dosage
INTEGRATE	 Local resistance, efficacy and cost-effectiveness

> Appropriate prescribing conforms to these criteria.



資料來源: Ball et al. Antibiotic therapy of community respiratory tract infections: strategies for optimal outcomes and minimized resistance emergence. J Antimicrob Chemother 2002; 49:31–40









課程結束

