

Overkoepelende Nieuwsbrief

Belgische Pediatrische Verenigingen

18 maart 2020

Opgesteld door de voorzitters:

Marc Raes

Tyl Jonckheer

An Bael

Pierre Philipet

Beste collega's

COVID 19 Information Général

De Covid 19 epidemie is nu helemaal in het land en als kinderartsen hebben wij twee taken: de beste zorgen verlenen aan alle kinderen in moeilijke omstandigheden en uzelf beschermen.

Er is een spontane groep Belgian paediatric CORVID19 groep (hoofdzakelijk pediatrische infectiologen en voorzitters van de pediatrische verenigingen) ontstaan die in zeer moeilijke omstandigheden zoveel mogelijk informatie verzamelt en tracht duidelijke richtlijnen uit vaardigen die u op de site van de overheid Sciensano kunt vinden.

Stay save,

Stay strong!

Vragen

U zult met veel vragen zitten. De antwoorden die u zult krijgen zullen met de dag evolueren. Wij beloven u regelmatig de meest recente informatie door te geven.



*It always
seems
impossible
until it's done*
Nelson Mandela

Essentiële boodschappen

Op de dag van vandaag wensen wij als voorzitters van de verschillende pediatrische verenigingen die constant met elkaar in contact zijn, de volgende essentiële boodschappen geven. Gesprekken met Italiaanse en Chinese kinderartsen hebben ons doen besluiten om dringend te communiceren.

1.

Als u niet beschikt over beschermingskledij (minstens masker, bril en handschoenen) mag u absoluut geen zieke kinderen (zowel respiratoir als digestief) onderzoeken.

2.

Organiseer zo snel mogelijk een proper circuit (= afdelingen en raadplegingen) waar kinderen zonder enige infectie klachten worden gezien en scheidt die volledig af van een 'covid 19' circuit waar alleen zieke kinderen worden gezien en zowel u als de verpleegkundigen op de meest veilige omstandigheden kunt werken.

3.

Doe zoveel mogelijk aan tele en video consultatie

4.

Wij benadrukken dat vaccinatie van kinderen essentieel is om te voorkomen dat door het stoppen hiervan wij in de nabije toekomst snel 'oude' infecties gaan terugzien zoals mazelen, pertussis, H influenzae... Wij doen er alles aan om met Kind en Gezin en huisartsenverenigingen hiervoor creatieve oplossingen te vinden.

5.

Wij moeten als kinderartsen ervoor waken dat de zorg aan onze chronische patiënten onverminderd kan doorgaan. Hiervoor ook zoeken wij creatieve oplossingen om deze zorg in propere circuits te laten doorgaan.



Informatie opgesteld door onze Zwitserse collega's



Steckbrief COVID-19 – Clinical characteristics in children and adolescents updated 18 March 2020

<http://www.kinderkliniken.insel.ch/de/coronavirus/>

Causative agent	SARS-CoV-2 ¹
Receptor	<ul style="list-style-type: none"> • Angiotensin-Converting Enzyme 2 (ACE2 receptor)² • convalescent sera from SARS-1 patients block SARS-CoV-2 entry via ACE2³
Transmission	<ul style="list-style-type: none"> • droplet, contact; aerosol? • ½ life in aerosol ~1 hour, ½ life on plastic/steel 6-8 hours (van Doremalen N, N Engl J Med 17/03/2020) and⁴ • viral transmission can start 1-2 days before the onset of symptoms («serial interval» < incubation period⁵; recovery of virus from NPA before onset of symptoms (Woelfel R, medRxiv)⁶ • viral RNA in NPA from children until 6-22 days after disease onset^{7,8} • viral RNA in feces from day ~5 to > 4 weeks after disease onset⁸⁻¹⁰ • viral load in NPA does not correlate with severity of COVID-19 in adults¹¹ • CDC recommends two consecutive negative RT-PCR tests within >24h before discontinuing isolation in hospitalized patients
Incubation period	4-6 days (range, 1 to >14 days)
Epidemiology	<ul style="list-style-type: none"> • basic reproduction rate R_0 2.2 (90% CI, 1.4-3.8)^{12,13} • high risk for «superspreader events» (dispersion parameter $k \downarrow$)¹³ • age <15 years: 0.9% of all cases (China CDC Weekly)^{14,15} • transmission to children mainly within families^{8,10,16} • mortality in symptomatic cases (adjusted case fatality rate) age 0-9 years, 0%; age 10-19 years, 0.25%; all ages, 1.5% (Riou J, medRxiv)
Clinical manifestations	<ul style="list-style-type: none"> • common: asymptomatic, e.g. in children of all ages¹⁷ [Dong Y] • common: fever (may be of short duration or absent)^{8,14,16-19} • common: cough^{8,17,19} • common: malaise, headache, myalgias • common: mild diarrhea^{8,10,14} [Dong Y] • infrequent: rhinorrhea, pharyngitis, wheezing^{8,14,16,19} [Dong Y] • co-infections reported (e.g. Influenza A/B, <i>M. pneumoniae</i>)¹⁷
Laboratory findings	<p><u>CBC differential, CRP, PCT, chemistry generally uncharacteristic</u></p> <ul style="list-style-type: none"> • common: leucopenia < 4.5 G/l; lymphopenia < 1.5 G/l, thrombocytopenia < 150 G/l^{14,19,20} • CRP/PCT at first presentation normal to moderately elevated^{8,17,19}



Microbiology	<ul style="list-style-type: none"> • RT-PCR from NPA (ifik, private laboratories and NAVI HUG Geneva) • seroconversion ~1 week after onset of symptoms (Woelfel R, medRxiv) • serum IgM/IgG tests under development, <u>not</u> routinely available²¹
Radiology	<ul style="list-style-type: none"> • conventional CXR: normal or non-specific findings • chest CT: unilateral or bilateral, uni- or multifocal, peripheral, commonly subpleural lesions; focal lesions typically with central consolidation and halo sign or ground glass opacities (GGOs)^{17,19,22} • <u>no</u> pleural effusion^{17,22} • <u>no</u> hilar lymphadenopathy^{17,22}
Clinical course	<ul style="list-style-type: none"> • common: asymptomatic (reported in infants^{7,8,16} and children^{8,23}) • common: upper respiratory tract infection (children and healthy adults)⁸ • common: pneumonia (with absent, mild or moderate clinical disease)^{17,19} • very rare: progressive lung disease with respiratory failure^{10,19}, reported in one study to be more common in infants [Dong Y] • <u>currently 1 pediatric fatal case in a 14-year-old reported</u> [Dong Y]
Clinical course - immunodeficiency	<ul style="list-style-type: none"> • severe disease in immunocompromised children has not been reported to date • mortality in adults with cancer is elevated (China CDC Weekly)
Clinical course - pregnancy	<ul style="list-style-type: none"> • infections reported mainly in 3rd trimester; characteristic complications have not been reported to date^{24,25} • no evidence for vertical transmission and fetal infection²⁵⁻²⁷
Clinical course - neonates	<ul style="list-style-type: none"> • asymptomatic infection in neonates (including normal chest CT) has been reported^{10,17,26} • complicated perinatal/postnatal courses among <u>non-infected neonates</u> of COVID-19 infected mothers have been reported²⁸
Treatment	<ul style="list-style-type: none"> • mainly supportive • currently no evidence from clinical trials available • drugs with antiviral activity against SARS-CoV-2 in vitro: remdesivir (nucleoside analog)^{29,30}, lopinavir/ritonavir (Kaletra®)³⁰, darunavir/ritonavir, chloroquine/hydroxychloroquine (Plaquenil®)³¹ • immunomodulation with tocilizumab (Actemra®, anti-IL6 mAb) reported • ACE2/viral entry blocker (TMPRSS2 inhibitors, e.g. Nafamostat) effective in vitro^{3,32} • <u>recommendations not to use NSAID (e.g. ibuprofen; upregulation of ACE2 receptor expression?) currently lack a firm scientific basis</u>
Prevention	<ul style="list-style-type: none"> • Inpatients: precautions according to Swissnoso/PIGS • Outpatients: precautions according to BAG, KAZA • Neonates: no separation of mother/child pairs (Swissnoso/PIGS, SGGG, WHO); <u>management according to local infection control policy</u> • IMPORTANT: scheduled routine immunizations in children ≤ 2 years of age should not be postponed (EKIF/BAG/SGP)

Team Kinderinfektologie (Pediatric Infectious Disease)

Inselspital, Universitätsklinik für Kinderheilkunde, Pädiatrische Infektiologie und Impfwissenschaften, CH-3010 Bern

Prof. Dr. med. Christoph Aebi, Chefarzt, Telefon +41 (0)31 632 12 99, christoph.aebi@insel.ch

Chefarztsekretariat: Barbara Mann, Telefon +41 (0)31 632 94 43, Fax +41 (0)31 632 94 16, barbara.mann@insel.ch

Poliklinik Tel. +41(0) 31 632 94 11 www.kinderkliniken.insel.ch



Literatuur

1. Jiang S, Shi Z, Shu Y, et al. A distinct name is needed for the new coronavirus. *Lancet* 2020.
2. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. *Nature microbiology* 2020.
3. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* 2020.
4. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *The Journal of hospital infection* 2020;104:246-51.
5. Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases* 2020.
6. Tong ZD, Tang A, Li KF, et al. Potential Presymptomatic Transmission of SARS-CoV-2, Zhejiang Province, China, 2020. *Emerging infectious diseases* 2020;26.
7. Kam KQ, Yung CF, Cui L, et al. A Well Infant with Coronavirus Disease 2019 (COVID-19) with High Viral Load. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2020.
8. Cai J, Xu J, Lin D, et al. A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2020.
9. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *Jama* 2020.
10. Cao Q, Chen YC, Chen CL, Chiu CH. SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics. *Journal of the Formosan Medical Association = Taiwan yi zhi* 2020.
11. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *The New England journal of medicine* 2020.
12. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *The New England journal of medicine* 2020.
13. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin* 2020;25.
14. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *The New England journal of medicine* 2020.
15. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507-13.
16. Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang ZJ. Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China. *Jama* 2020.
17. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. *Pediatric pulmonology* 2020.
18. Chen ZM, Fu JF, Shu Q, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. *World journal of pediatrics : WJP* 2020.



INSELSPITAL

UNIVERSITÄTSSPITAL BERN
HOPITAL UNIVERSITAIRE DE BERNE
BERN UNIVERSITY HOSPITAL

21. Li Z, Yi Y, Luo X, et al. Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis. *Journal of medical virology* 2020.
22. Li W, Cui H, Li K, Fang Y, Li S. Chest computed tomography in children with COVID-19 respiratory infection. *Pediatric radiology* 2020.
23. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514-23.
24. Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know. *American journal of obstetrics and gynecology* 2020.
25. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020;395:809-15.
26. Lu Q, Shi Y. Coronavirus disease (COVID-19) and neonate: What neonatologist need to know. *Journal of medical virology* 2020.
27. Li Y, Zhao R, Zheng S, et al. Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China. *Emerging infectious diseases* 2020;26.
28. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Translational pediatrics* 2020;9:51-60.
29. Sheahan TP, Sims AC, Leist SR, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nature communications* 2020;11:222.
30. Martinez MA. Compounds with therapeutic potential against novel respiratory 2019 coronavirus. *Antimicrobial agents and chemotherapy* 2020.
31. Yao X, Ye F, Zhang M, et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2020.
32. Yamamoto M, Matsuyama S, Li X, et al. Identification of Nafamostat as a Potent Inhibitor of Middle East Respiratory Syndrome Coronavirus S Protein-Mediated Membrane Fusion Using the Split-Protein-Based Cell-Cell Fusion Assay. *Antimicrobial agents and chemotherapy* 2016;60:6532-9.

