#Escv2016-Fouchier wild birds major reservoirs #influenza #paramyxoviruses #coronavirus pandemic potential

http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20840#escv2016 ...

#ESCV2016-Fouchier H7N9 intermediate transmissible among ferrets, in between pandemic and non-transmissible strains http://www.ncbi.nlm.nih.gov/pubmed/23925116

#ESCV2016-Fouchier Kawaoka's and Fouchier's lab found comparable HA mutations in ferret-transmitted H5N1. Fig 3 http://www.ncbi.nlm.nih.gov/pubmed/26385895

#escv2016 #GOF studies underpins virus genome sequencing and phenotyping surveillance programs – safety a key feature

#escv2016 Avian influenza A(H10N7) in harbour seals showed similar traits http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20967 ... Receptor not yet identified

#escv2016 H7N9 emerged (China) & had some of the GOF mutations (PB2 and HA) present but had limited transmissibility

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3819191/ ...

#escv2016 stable HA (activation pH  $\leq$  5.5) needed for pH1N1 pathogenicity and airborne transmissibility in ferrets http://www.pnas.org/content/113/6/1636.abstract ...

#escv2016 Mutations associated with #GOF in influenza have been identified - http://jvi.asm.org/content/early/2016/04/07/JVI.00130-16 ... http://femsre.oxfordjournals.org/content/40/1/68

#escv2016-Fouchier transmission models can confirm or disprove importance of point mutations in viral strains http://science.sciencemag.org/content/336/6088/1534.full ...

#escv2016 ferrets are excellent models for study of influenza transmission and #GOF http://science.sciencemag.org/content/325/5939/481 ... https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4003409/ ...

#escv2016 MERS: ancient bat to African camels, trade to ME and amplified by farming. Young males infected, some admitted and trigger HAI.

#escv2016-Drosten In KSA, MERS viral load in resp tract already very high on admission http://www.ncbi.nlm.nih.gov/pubmed/26565003 Virtually no virus in stool.

#ESCV2016-Drosten Asymptomatic MERS patients shed virus in low amounts, Ct-values 35-40. Patients shed much more, Ct 15-20 2% in shepherds, 3% in slaughter workers http://www.ncbi.nlm.nih.gov/pubmed/25863564

#escv2016 Lab surveillance data shows high viral loads from patients seen in large A&Es – scope for transmission. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4303774/ ...

#escv2016 seroprevalence rural bias https://epidemio.wivisp.be/ID/Documents/Seminar/SSID\_2016/MERS\_COV.pdf .... Antibodies last about 5-10 years = 40000 people infected in KSA in 5 - 10 yrs

#escv2016 MERS a pan-African & linked to camels.On-going problem rooted back to a conspecific virus from African bat

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4178802/ ...

#escv2016 bats were proposed initially as reservoir

http://wwwnc.cdc.gov/eid/article/19/11/13-1172\_article ... but middle-east link suggested otherwise http://epidemic.bio.ed.ac.uk/

#escv2016-Drosten >1800 cases ~640 fatalities (2Sep16 WHO). Clusters - hospital outbreaks lasting ~ 3 months but transmission is on-going.

#escv2016-Pankuweit Parvovirus and HHV6 most common viruses in cardiac tissue of myocarditis patients. But what about causality???

#escv2016-Pichon presents beautiful example of a clinical case of congenital CMV infection and 'placentitis'

#escv2016 Interested in HCMV, from experimental and clinical point of view, visit the next CMV meeting in Holland, 2017 http://www.cmv2017.nl

#escv2016-Vossen The longterm sequelae of congenital CMV were more severe in children that were already symptomatic at birth

#escv2016-Vossen Next to hearing loss, CROCUS showed also more motor and cognitive impairment among congenital CMV-infected children

#escv2016-Vossen The Dutch CROCUS study analyzed in retrospect the presence of congenital CMV infection in a large birth cohort (70,000)

#escv2016-Vossen Also congenitally CMV-infected babies without symptoms at birth can develop longterm sequelae

#escv2016-Kowalik Adoptive transfer of CMV-specific T-cells dramatically affected the CMV sequence diversity within compartments

#escv2016-Kowalik congenital HCMV sequences differentiate by tissue compartment, for instance urine vs. blood http://ncbi.nlm.nih.gov/pubmed/?term=diversity+cmv+renzette ...

#escv2016-Kowalik HCMV populations (DNA virus) are as diverse as RNA virus populations http://www.ncbi.nlm.nih.gov/pubmed/?term=diversity+cmv+renzette ...

#escv2016-Kowalik CMV is the leading cause of infection-related birth defects

#ESCV2016-Kowalik Individuals are often infected with a multiplicity of CMV genotypes http://www.ncbi.nlm.nih.gov/pubmed/23694837

#escv2016 Leruez-Ville Predicting fetal outcome in cCMV is possible http://www.ncbi.nlm.nih.gov/pubmed/27063062

#escv2016 Leruez-Ville Avidity results can be unreliable where CMV IgG is low.

#escv2016 Leruez-Ville Saliva more likely to give false positive CMV due to low copy contamination from genital secretions or breast milk.

#ESCV2016-Goldstein HA phylogenetic tree from whole genome NGS (illumina) reflected HA-only tree, based on >100 flu samples from Scotland

#escv2016 M-RT-PCR amplified seqments for flu WGS http://www.ncbi.nlm.nih.gov/pubmed/22528160 provides outbreak resolution and resistance mutation advantages

#ESCV2016-Pechirra Most rhinovirus A detections in Portugal were form adults (15-44 yrs). Often associated with cough and myalgia

#ESCV2016-Pechirra In Portugal, 45% of detected seasonal rhinovirus belong to species A, 15% to B and 40% to C.

#escv2016-Cantais Rapid (15m) influenza POCT in paediatric AE reduced additional laboratory tests, prescriptions and lumbar punctures.

#ESCV2016-Shindo A big thank to the clinical virologists that took part in the diagnostic field labs fighting ebola

#escv2016 Shindo WHO ERC pre-approved natural history prepared to help initiate research protocols

#escv2016-Shindo WHO undertake significant training including mentorship in ETU

#escv2016-Shindo WHO has 3 aims – Governance Guidance Research

#escv2016-Shindo WHO earning the trust of the community is critical

#escv2016-Shindo WHO creating expert networks to counter emerging infections. Posts will be advertised in due course

#ESCV2016-Piralla. Increase in TTV load in kidney transplant patients was independent of used immunosuppressive regimen

**#ESCV2016**-Piralla. TTV can be detected in 90% of population, without any symptoms. TTV load increases with impaired immunity.

#ESCV2016-Pichon. In retrospect, most Enterovirus D68 cases in Lyon region were noted in 2012 and 2014, with genogroup B replacing A

#escv2016-Heim ADV New types may appear that cannot be monitored by blood testing - as single system infections may appear.

#escv2016-Heim ADV New species in 54 year old SCT – low level blood. Encephalitis. Species D. Highly recombinant.

#escv2016-Heim ADV In post-transplant children usually species C.

#escv2016-Heim ADV can be referred to as serotypes or genotypes. Most new types are species D.

#escv2016-Guiomar D68 pilot of children <18y with severe RTI or neuro illness – 29 enterovirus, 20 (69%) D68. <1m – 6y.2 neurological /AFP

#escv2016-Guiomar D68 Portugal 2015 retrospecive – 2.6% Ev-D68 positive respiratory symptoms identified

#escv2016-Guiomar D68 Large outbreaks 2014/15 with severe respiratory symptoms with 4 deaths - US

#escv2016-Guiomar D68 Isolated California 1962. Polio like presentations appeared California 2112/13

#escv2016-Slavov Zika joint pain rash low grade fever fetal microcephaly – first autochthonous case Brazil 2015

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4501423/ ...

#ESCV2016-Slavov. Presents atypical symptomatology in children that includes peritonitis

#escv2016-Bottcher #ev71 has accepted geno-grouping . C1 became the dominant strain in 2016 in Germany

#escv2016-Azevedo V1/V2 shields VP3 hypervariable region, is a target for neutralisation antibody, reducing reduces viral replication

#ESCV2016-Azevedo. HIV2 uses a broader range of coreptors, which paradoxically handicaps HIV2, since non-permissive cells are also hit

#escv2016-Azevedo CD4 independent HIV-2 strains exist and have a wider tropism – but binding site neutralisd by antibodies

#escv2016-Azevedo CCR5 CXCR4 are main co-receptors for hIV-2 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3074590/ ...

#escv2016-Azevedo #HIV-2 Less virulent http://www.ncbi.nlm.nih.gov/pubmed/7915856

#ESCV2016-Meijer. In the coming years the HPV-vaccination program and the cervical cancer screening program need to be tuned (in NL)

#ESCV2016-Meijer. Posiitve hrHPV testing in the population screening is followed by cytology, to increase specificity

#ESCV2016-Meijer. Half of the cervical cancer cases in the Netherlands did not attend the cervical cancer screening program

#ESCV2016-Meijer. Above 40 years of age, with repeatedly negative hrHPV-testing, the screenings interval can be extended to 10 yrs (in NL)

#escv2016-Meijer DNA methylation analysis on HPV-test-positive self-samples non-inferior to cytology CIN2 or worse http://www.ncbi.nlm.nih.gov/pubmed/24529697

#ESCV2016-Meijer. Therefore use test hrHPV with 'suboptimal' analytical sensitivity, but optimal clinical sensitivity

#ESCV2016-Meijer. hrHPV-testing in the context of cervical cancer screening should detect only transforming infections

#escv2016-Meijer #HPV Triage strategy depends on resources http://www.ncbi.nlm.nih.gov/pubmed/21400507

#ESCV2016-Meijer. Over half a million new cases of HPV-induced cervical cancer a year. That's a lot, especially as it is largely preventable

#ESCV2016-Meijer. hrHPV infections can be divided in productive (majority) and transforming infections (rare, risk of cervical cancer)

#escv2016-Solis #bkv – The strain causing the viraemia is in post transplant nephropathy is donor dervived.

#escv2016-Solis Higher post transplant neut assays before transplant have lower risk of nephropathy

#escv2016-Solis #bkv neutralisation assay used for seroanalysis during kidney transplantation

#escv2016-Marongiu maxRatio is a robust alternative to cycle threshold https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2504305/ ...

#escv2016-Thielen Every step in NGS – including enzyme use – can introduce variations more readily than seen in Sanger sequencing

#ESCV2016-Thielen NGS provides so much data, we simply do not have the resources to analyze them all

#ESCV2016-Thielen Consider APOBEC filtering when performing bioinformatic analysis of NGS HIV resistence data using NGS are not that high, but you need a bioinformatician!

#escv2016-Thielen minion can sequence HIV in minutes, portable, but 15-20% error rate - so needs improved bioinformatics for more accuracy

#escv2016-Thielen Low load sequencing becoming more frequent and use of proviral DNA may introduces errors – need for Apobec filter

#escv2016-Thielen many soft ware bioinformatics packages are free on-line but usually written for Linux

#escv2016-Daumer HGS reagent costs for HIV around €92 – then you need a bioinformatician

**#ESCV2016**-Daumer Sensitivity to detect minor variants increases dramatically compared to Sanger seq. But what is the clinical relevance??

#ESCV2016-Daumer NGS especially promising for virus typing and antiviral resistance mapping

<u>#ESCV2016</u> EV-D68 caused significant morbidity with cases of paralysis in Wales over 2016 winter

<u>#ESCV2016</u>-Moore shows impressive ev68 paralysis cases. Call for EU non polio surveillance increases

#escv2016-Wolthers Results of the mariPOC-gp study is revealed in poster #221, so can't tell you the results now :-((

<u>#escv2016</u>-Wolthers The AEROpico project placed mariPOCs in the gp's office. Patients liked it immediately, gap's bit reluctant

Fast typing of Rhinovirus in 1 hour - <a href="Mailto:@K3Wolthers">@K3Wolthers</a> at <a href="#ESCV2016">#ESCV2016</a> - impressive

<u>#escv2016</u>-Pas The future – POCT / Realtime Hub / NGS

<u>#escv2016</u>-Pas Realtime genotyping became important for ebole http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21270 ... #escv2016-Pas value of external quality demonstrated for MERS http://www.ncbi.nlm.nih.gov/pubmed/26209385

#escv2016-Pas Molecular diagnostic preparedness requires early data sharing, like http://www.ncbi.nlm.nih.gov/pubmed/27516635 and http://www.who.int/bulletin/online\_first/16-175950.pdf ... #zika

#escv2016-Pas European Virus Archive EVA makes viral strains available for non commercial labs for validation.

#escv2016-Pas Upscaling labs - could practical concept for sharing workloads as part of outbreak response

<u>#escv2016</u>-Pas Collaboration critical for new diagnostic challenges http://www.who.int/bulletin/online\_first/16-175950.pdf ...

<u>#escv2012</u>-Pas from Rotterdam EMC receives the Abbott-Award for contributing to molecular diagnostics <u>#congrats</u>

#escv2016-Pas European Virus Archive EVA makes viral strains available for non commercial labs for validation. Marion Koopmans added, Check the site @EVAg EU

#ESCV2016-Van Leer. CMV resistance mutations in SOTs associated with high peak load (>100,000), prolonged treatment (>6 m), primary infection

#ESCV2016-Martin. IFN-gamma inhibits BK-polyomavirus replication in an JAK/STAT dependent manner

#ESCV2016-Corti. Broadly reactive neutralizing antibody against Flu A more potent that the neuraminidase inhibitors (no data shown)

#ESCV2016-Corti. Also for Flu A (HxNx) potentially suitable to be treated with broadly reactive antibodies http://www.ncbi.nlm.nih.gov/pubmed/21798894

#ESCV2016-Corti. Specificity, cross-reactivity, and function of antibodies elicited by Zika virus infection http://www.ncbi.nlm.nih.gov/pubmed/27417494

#ESCV2016-Corti. Mode of action of broadly reactive neutralizing antibody recognizing all influenza A subtypes http://www.ncbi.nlm.nih.gov/pubmed/27453466

#escv2016-corti MEDI8852 mAb has potential for immunotherapy in influenza virus-infected humans http://www.cell.com/cell/pdfExtended/S0092-8674(16)30720-6 ...

#escv2016-corti cross reactive influenza viruses should target both group 1 and 2 viruses

#ESCV2016-Corti. Rabies is excellent candidate for post-exposition prophylaxis with broadly reactive antibodies http://www.ncbi.nlm.nih.gov/pubmed/26992832

#escv2016-corti cross reactive antibodies may be protective or enhancing – http://science.sciencemag.org/content/early/2016/07/13/science.aaf8505 ...

#escv2016-corti broadly reavtive mAbs may extend the theraputic range across viruses http://www.ncbi.nlm.nih.gov/pubmed/21798894 flu http://www.nature.com/nature/journal/v501/n7467/abs/nature12442.html ...

#ESCV2016-Templeton. The myCAP study, syndromic testing using broad range (bad and vir) respiratory multiplex PCR http://www.ncbi.nlm.nih.gov/pubmed/26747825

**#ESCV2016**-Templeton. Broad range viral respiratory PCR provides enormous amount of information and contributes to reduced use of antibiotics

#ESCV2016-Templeton. RSV not only in the very young, also adults >50 yrs are frequently hit

#escv2016-templeton Comprehensive molecular testing significantly improves pathogen detection in CAP

#escv2016-Hosjnak Seroprevalence HDV in Slovenia (0.23%). 3 patients – all showed recovery of infection.

#escv2016-martro hcv identification of minority variants by WGS may allow personalised targeting of DAA treatment -cut-off at 15%

#escv2016-nascimento hev HepeCONTROLL http://hepecontrol.weebly.com/ work funded through grant support http://www.eeagrants.gov.pt/

#escv2016-nascimento hev 19/2115 Portuguese blood donors Jul15-Jan16 HEV RNA positive. 12/19 seronegative ? false positives PCR

#escv2016-Baumert CLDN1 target in HCV infection. Can be blocked by MAbs. Effective against DAA-Resis strains. Monotherapy with no resistance

#escv2016-Baumert hcv works through EGF receptor and later cells linked to proliferation. EGF also associated with HCC development

#escv2016-Baumert hcv still challenges access to affordable treatment, preventing progression to HCC after virus cleared after fibrosis

#escv2016-houldcroft ADV in children. Hexon WGS sufficient to exclude transmission but needs epidemiological data also for transmission.

#escv2016-gimenez High TTV post transplant may reflect proinflammatory response as GVHD and may act as a marker for immune reconstitution

#escv2016-Tabatabai IVIG use in SCT patients with prolonged RSV shedding induced stop codons in G with loss of 72aa and escape mutants.

Hepatitis E virus: Assessment of the epidemiological situation in Europe, 2014/15 #ESCV2016 http://bit.ly/2cr5aoU

#escv2016 EPS TTV has potential for post transplant monitoring https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4404260/ ... after first 60 days HEV transmits to transplant patients, becomes chronic http://www.ncbi.nlm.nih.gov/pubmed/21354150 and need treatment

#escv2016 EPS potential for pretransplantation BKPyV serological testing of (potential) donors and recipients http://onlinelibrary.wiley.com/doi/10.1111/ajt.13880/abstract ...

#escv2016 EPS BKV monitoring post renal transplant also advised http://www.ncbi.nlm.nih.gov/pubmed/23465010

#escv2016 EPS ebv PTLD 85% of Eurpoen lab do EBV monitoring http://www.ncbi.nlm.nih.gov/pubmed/25686696 no agreement on cut-offs

#escv2016-baldanti Combined molecular and immunological monitoring is useful for risk stratification and should become routine.

#escv2016-baldanti cmv PET if repeated treatments are necessary then antiviral resistance can emerge. http://jac.oxfordjournals.org/content/52/3/324.full ...

#escv2016-baldanti cmv PET needs reliable diagostics – plasma and whole blood rise and peak together but plasma loads declines slower

#escv2016-baldanti cmv prevention can use PET or prophylaxis http://onlinelibrary.wiley.com/doi/10.1111/tri.12629/abstract ...

#escv2016-baldanti cmv SCT immune dysfunction short lived (1y); SOT – mild suppression but prolonged impacts CMV http://www.ncbi.nlm.nih.gov/pubmed/25896527

#escv2016-gustavsson noro fast clearance (<14 days) seen in established strains, slow clearance (>14 days) a feature of new strains

#ESCV2016-Gustavsson. Duration of norovirus shedding increased (>14 d) in patients infected with local Gothenburg GII.4 strain

#escv2016-gustavsson noro new gll.4 strains emerge ever ~ 2-4 years New Orleans 2010 Sydney 2012

#ESCV2016-Brown. No. of (London/UK?) hospital admissions seems of influence to no. of norovirus cases, might explain 50% of the noro cases

#escv2016-brown noro different seasonal trends in hospital versus community https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2873766/ ...

#ESCV2016-Kroes. Endonuclease-treatment of cardiac tissue might discriminate between B19 DNA-remnants and virus with protective capsid

#ESCV2016-Kroes. B19-viremia often 'only' DNAemia, as shown in Dutch blood bank donors (Molenaar, J Clin Virol 2016, in press).

#ESCV2016-Kroes. Tissue persistence of B19 is a common feature of erythrovirus genomes. Useful in archeovirological studies (mummies etc)

**#ESCV2016**-Kroes. High prev of B19 DNA in myocardial autopsy samples from subjects without myocarditis/cardiomyopathy

http://www.ncbi.nlm.nih.gov/pubmed/?term=schenk+parvovirus ...

#ESCV2016-Kroes. Indeed B19 DNA is found in myocardial tissue, but also regularly found in healthy tissue http://www.ncbi.nlm.nih.gov/pubmed/17452164

#ESCV2016-Kroes. Several other diseases have been associated with B19, solely based on detection of B19 DNA in affected tissue, esp cardial

#ESCV2016-Kroes. Severe B19 anemia is seen in immunocompromised patients and those with hemoglobinopathies

#ESCV2016-Kroes. B19 parvovirus replicates exclusively in erythroid precursor cells, can therefore cause anemia. When in fetus --> hydrops

#ESCV2016-Harvala. EV type-specfic antibodies needed for typing of culture isolates become more and more difficult to obtain (commercially)

#ESCV2016-Harvala. @ECDC\_EU performed survey of the presence and type of enterovirus across Europe among EU laboratories (questionnaire)

#escv2016-harvala most European countries many now use molecular techniques for surveillance http://www.ncbi.nlm.nih.gov/pubmed/25039903

#escv2016-harvala questionnaire with ECDC and WHO for surveillance survey - 29/30 European countries replied

#escv2016-harvala need for better surveillance of current and emerging enteroviruses - >116 types - important cause of significant morbidity

#ESCV2016-Muscat. With increasing measles vaccine coverage vaccine failure (non-responders) becomes more apparent, as denominator rises#escv2016 harvala enterovirus

surveillance – important to include respiratory samples as well as blood, csf and stool to allow for D68

#escv2016-muscat measles progress has been made towards elimination http://www.euro.who.int/\_\_data/assets/pdf\_file/0019/305164/elimination-status-EN.pdf?ua=1 ...

#escv2016-muscat measles – better information, vaccinology in curricula, school based learning, better communication, promotion, championing

#escv2016-muscat WHO Measles Surveillance - better reporting, typing, operational procedures for epidemiological and laboratory procedures

#escv2016-muscat WHO we need to have vaccine advocates http://tinyurl.com/h7yff9b

#escv2016-muscat measles vaccine level should be >95% - but many issues, delays, misleading information, poor access

#escv2016-muscat measles challenge – commitment, vaccination, close gaps, surveillance, education

#escv2016-muscat measles at risk groups – anthroposophic schools, travellers, unvaccinated, some religious groups http://www.euro.who.int/\_\_data/assets/pdf\_file/0019/262009/EpiBrief-Issue-3,-2014.pdf?ua=1 ...

#escv2016-muscat WHO immediate aim is to eliminate #measles rather than eradicate it like happened with smallpox