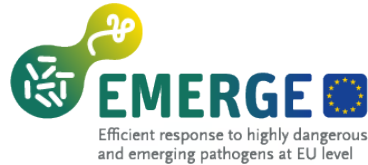




ARISTOTLE
UNIVERSITY OF
THESSALONIKI



HELLENIC CENTER FOR
DISEASE CONTROL & PREVENTION
MINISTRY OF HEALTH



Efficient response to highly dangerous
and emerging pathogens at EU level



Health Conference
Best practices in implementing
the International Health Regulations

Laboratory preparedness to highly dangerous and emerging pathogens: the Greek experience

Prof. Anna Papa, MD, PhD
Aristotle University of Thessaloniki, Greece

Tasks of the National Reference Centre for Arboviruses & Hemorrhagic Fever viruses

- To test clinical and arthropod vector samples in order to detect arboviruses and viruses capable to cause hemorrhagic fever in humans, including clinical samples from imported cases
- To genetically characterize the detected viruses
- To identify the genetic relationships with respective strains circulating worldwide (phylogenetic analysis)
- To detect outbreak situations
- To be prepared for detection of high and/or emerging pathogens
- To report cases to Public Health authorities
- To collaborate with KEELPNO (24/7) for the response to public health events in order to contain the spread of diseases.

Pathogens

- Arboviruses (e.g. West Nile virus, Toscana and other phleboviruses)
- Highly dangerous viruses (hemorrhagic fever v.: hantaviruses, CCHFV, Ebola and other Filoviruses, Lassa and other Arenaviruses)
- Emerging (e.g. West Nile virus)
- Imported (Zika, Chikungunya, Dengue, Yellow Fever, etc)
- Other pathogens which may be included in the differential diagnosis (e.g. leptospira, rickettsiae)

Diagnostic approaches

- Serology (better in >1 sample)
- Molecular methods (acute phase)
- Confirmation and typing by sequencing
- Next Generation Sequencing (NGS)



FROM SUSPICION TO CONFIRMATION

1. COMMUNICATION WITH THE CLINICIANS

about time, place and epidemiological characteristics
clinical symptoms and suspected pathogens



2. SAMPLING

identify which sample is the best for each specific syndrome and think critically for planning the sampling depending on the affected system

(sometimes brainstorming discussions in the case of non-typical picture)



3. TRANSPORTATION

Give instructions how to collect, label, package and transport samples appropriately and safely

4. PLANNING THE TESTING AND TEST!

- Perform the tests requested by sender
- Perform diagnostics for syndromes/clinical description (laboratory initiative)

Syndromic approach Collection and analysis of all available meta-data



Expert Review of Anti-infective Therapy

ISSN: 1473-7210 (Print) 1744-8336 (Online) Journal homepage: <http://www.tandfonline.com/loi/ierz20>

Challenges in laboratory diagnosis of acute viral central nervous system infections in the era of emerging infectious diseases: the syndromic approach

Anna Papa, Tzimoula Kotrotsiou, Elpida Papadopoulou, Chantal Reusken, Corine GeurtsvanKessel & Marion Koopmans

- Demographic data
- Clinical signs and symptoms
- Days after onset of the symptoms
- Place of residence, living conditions, occupation, recreational activities
- Underlying diseases/disorders / comorbidities
- Recent transfusion/ transplantation
- Immune status
- Vaccination history
- Recent travel in endemic areas
- Vector bite history

4a. QUALITY CONTROL AND BEST PRACTICE

Methods have to be validated via External Quality Assurance exercises to ensure the highest quality of tests.

Through projects, like EMERGE, EVD-LabNet (former ENIVD), or WHO

EQAs for Hantaviruses, Dengue v., Lassa v.,
Filoviruses, Orthopox viruses, SARS v., MERS
v., WNV, TBEV, CHIKV, Yellow fever v, Zika v.

Syndromic EQAs

Neurotropic viruses (EVD-LabNet)

High pathogens (EMERGE)

Metagenomics (EMERGE)

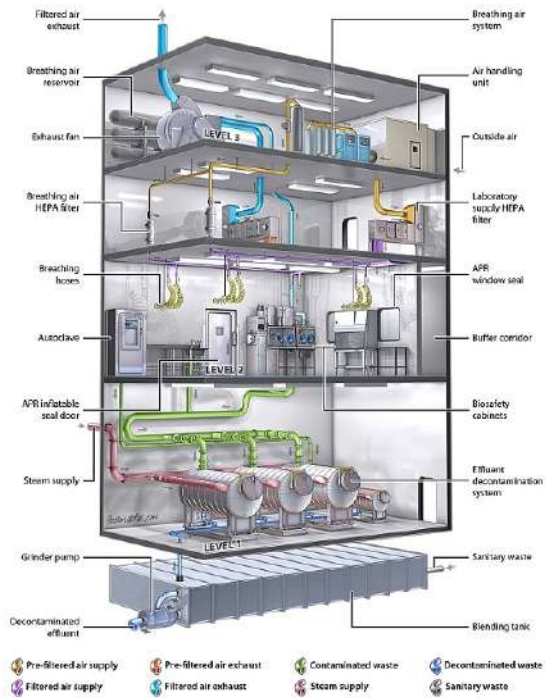


4b. Laboratory biosafety and biosecurity

Culture of safety

You should obey the rules!

They differ in technology complexity but they are similar:
work on high pathogens with good ORDER based on appropriate LOGISTICS



5. INTERPRETATION OF RESULTS



Take into account the test sensitivity and specificity, cross-reactivity
Think critically in relation to the disease and the patient immune status

Gray zone: SERIAL SAMPLE is required

Think critically if the identified pathogen is the responsible pathogen (special attention to the NGS results!)

6. REPORT AND DOCUMENTATION THE RESULTS

To the clinician

To Public Health authorities



Attention when the result is not confirmed.

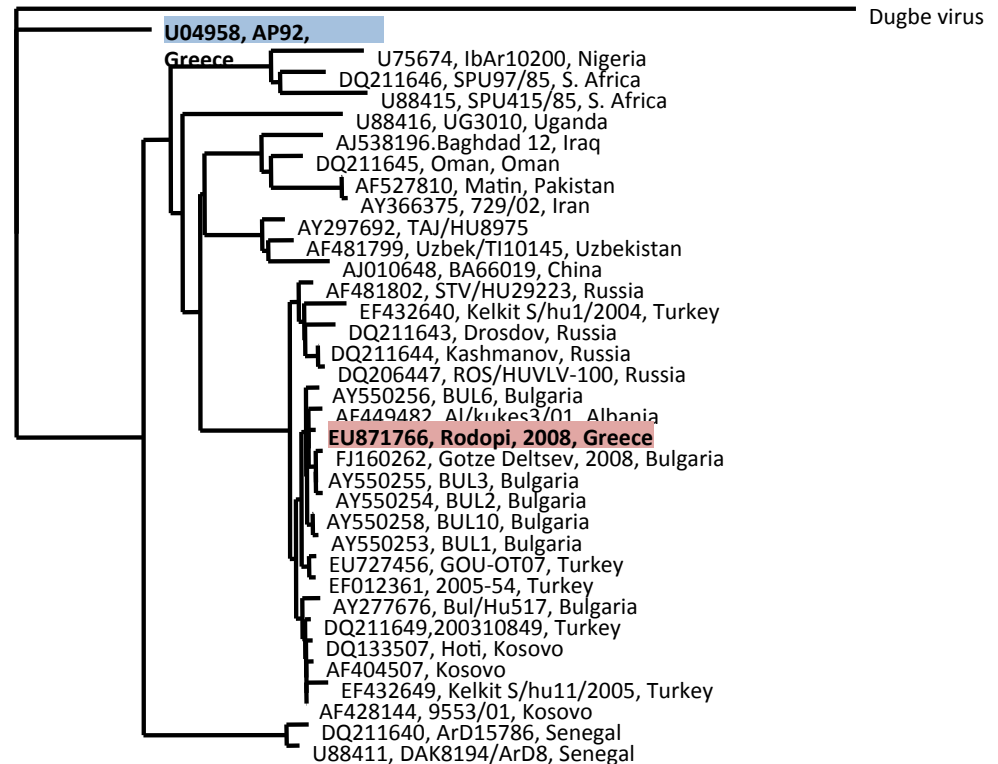
Laboratory diagnosis of the first CCHF case in Greece

Rapid communications

A CASE OF CRIMEAN-CONGO HAEMORRHAGIC FEVER IN GREECE, JUNE 2008

A Papa (annap@med.auth.gr)¹, H C Maltezou², S Tsiodras², V G Dalla³, T Papadimitriou², I Pierroutsakos², G N Kartalis³, A Antoniadis¹

June 2008; 46-year-old woman . No travel abroad. Agricultural worker. Tick bite. Fever, hemorrhage. Outcome: fatal.



Identification of WNV as causative agent of the first outbreak in Greece

2010

August 4. Physician from the Infectious Diseases Hospital in Thessaloniki, Greece:

“We observed an **unusual high number of encephalitis cases** during July”.

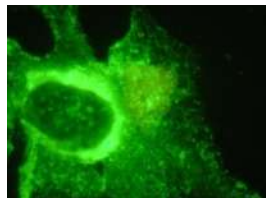
August 5. Samples from 11 patients with meningitis/encephalitis arrived at the lab. Phlebovirus negative.

August 6. WNV IgM antibodies detected in 10/11 patients by ELISA and IFA.

August 7. Four different PCRs resulted negative.

Ask the mosquito control company to collect for us mosquitoes from the gardens of the patients.

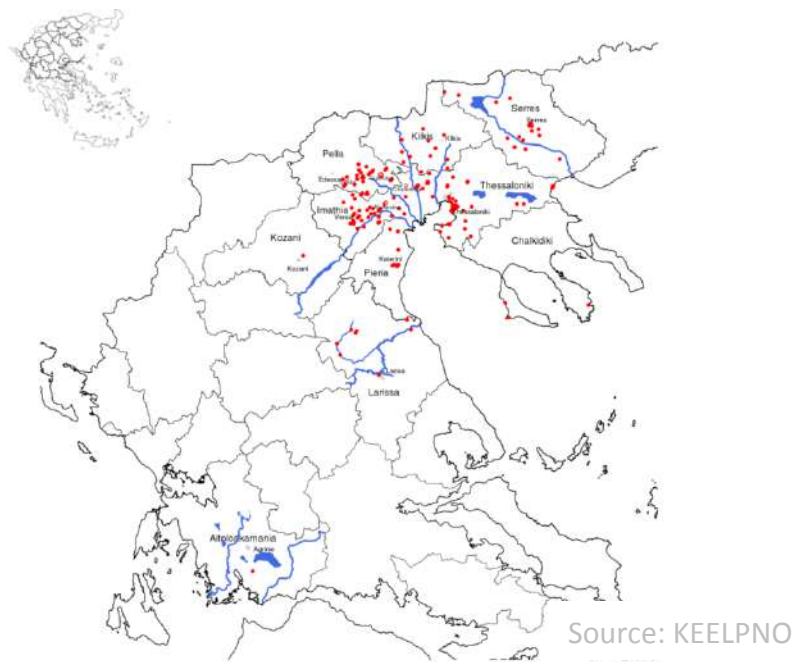
August 12. A pool of *Culex* mosquitoes collected at the garden of a patient in Nea Santa proved positive for **WNV lineage 2**.



RAPID COMMUNICATIONS

Ongoing outbreak of West Nile virus infections in humans in Greece, July – August 2010

A Papa¹, K Danis (daniscostas@yahoo.com)¹, A Baka², A Bakas³, G Dougas¹, T Lytras², G Theocharopoulos², D Chrysagis², E Vassiliadou², F Kamaria², A Liona², K Mellou², G Saroglou², T Panagiotopoulos^{2,4}

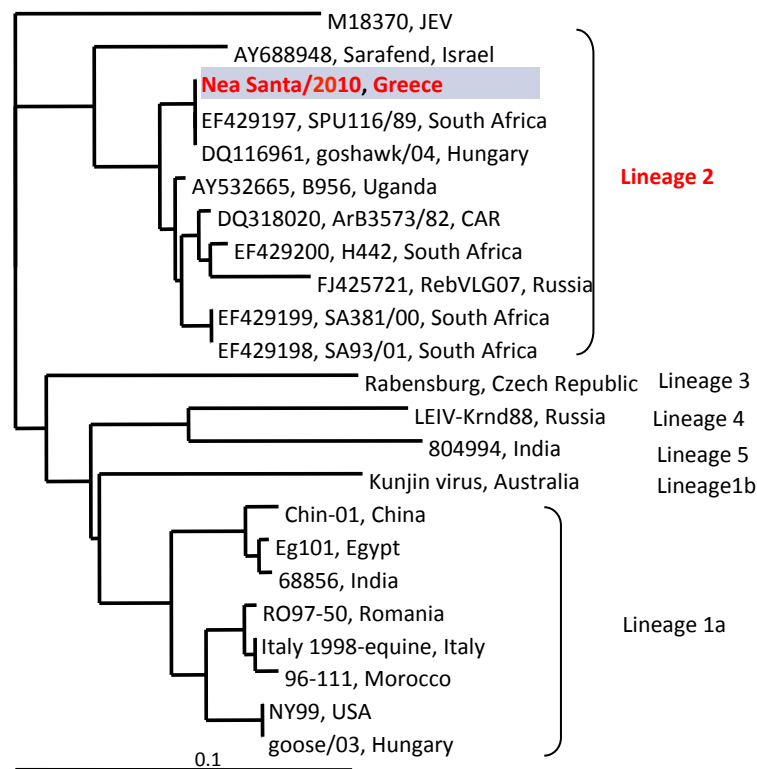


191 neuroinvasive cases, 33 fatal.

Detection of West Nile virus lineage 2 in mosquitoes during a human outbreak in Greece

A. Papa¹, K. Xanthopoulou¹, S. Gewehr² and S. Mourelatos²

1) Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki and 2) Eco-Development, S.A., Thessaloniki, Greece



Prompt laboratory diagnosis of imported cases (Zika, Dengue, Chikungunya)

Case report

Zika virus infection in a newly married Greek couple

Petros Ioannou^{a,*}, Stella Soundoulounaki^a, Nikolaos Spernovasilis^a, Elpida Papadopoulou^b,
Anna Papa^b, Achilleas Gikas^a

^a Department of Internal Medicine & Infectious Diseases, University Hospital of Heraklion, Heraklion, Crete, Greece

^b Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece



ZIKV infection poses a threat for public health worldwide, since returning travelers could be carriers of the virus, leading not only to risk of neurologic birth defects for their offspring, but also to risk of virus transmission in their country by local *Aedes* mosquitoes.

Laboratory diagnosis of an imported CCHF case, 6 June 2018

26.5.2018, Tick bite in Bulgaria

27.5.2018, onset of symptoms (headache, myalgia) visit the local hospital

30.5.2018, return to Greece and admission to the local hospital. Severe thrombocytopenia.

1.6.2018, transfer to a University hospital

4.6.2018, communication with the Head of the Ref. Centre who suspected CCHFV infection and informed KEELPNO. Immediate response: guidelines for personal protection of personnel; ribavirin was given to HCWs who had close contact.

6.6.2018 at 11.30, blood and serum samples arrived to the Reference Centre

6.6.2018 at 14.30, CCHFV infection confirmed by real-time RT-PCR and detection of IgM antibodies

6.6.2018 afternoon. Detailed medical history taken and message prepared to be sent to Bulgaria regarding awareness and tick protection

Benefits from participating in the EMERGE project

- Collaboration with other scientists working on high pathogens: exchange of knowledge and experience, share protocols, know whom to contact during a difficult situation
- Annual meetings, Working group meetings (high quality presentations, discussions, networking)
- EQAs on high pathogens, syndromic EQA and EQA using next generation sequencing
- Training

Expect the
Unexpected



*Effective disease **surveillance and reporting** are key strategies in any attempt to control the spread of a serious disease
Collaboration is the only way forward in tackling emerging diseases.*

Cross-border collaborations on high pathogens

Eur J Clin Microbiol Infect Dis (2002) 21:603–606
DOI 10.1007/s10096-002-0770-9

ARTICLE

A. Papa · S. Bino · A. Llagami · B. Brahimaj
E. Papadimitriou · V. Pavlidou · E. Velo · G. Cahani
M. Hajdini · A. Pilaca · A. Harxhi · A. Antoniadis

Crimean-Congo Hemorrhagic Fever in Albania, 2001

Genetic Detection of Dobrava/ Belgrade Virus, Bulgaria

Anna Papa and Iva Christova

DISPATCHES

Genetic Detection and Isolation of *Crimean-Congo hemorrhagic fever virus*, Kosovo, Yugoslavia

Anna Papa,* Bojana Bozovi,† Vassiliki Pavlidou,*
Evangelia Papadimitriou,* Mijomir Pelemis,‡
and Antonis Antoniadis*

Hantaviruses in Serbia and Montenegro

Anna Papa,* Bojana Bojovic,†
and Antonis Antoniadis*

Crimean-Congo Hemorrhagic Fever in Bulgaria

Anna Papa,* Iva Christova,†
Evangelia Papadimitriou,*
and Antonis Antoniadis*

Viral Load and Crimean-Congo Hemorrhagic Fever

Scandinavian Journal of Infectious Diseases
2008, 1–3, iFirst article

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SHORT COMMUNICATION

Suspected Crimean Congo Haemorrhagic Fever cases in Albania

Seroprevalence of Crimean-Congo Hemorrhagic Fever Virus, Bulgaria

Current projects and Networks



Efficient response to highly dangerous and emerging pathogens at EU level (Networking, rapid detection, training, EQAs)



Aim of COMPARE is the rapid identification, containment and mitigation of emerging infectious diseases and food borne outbreaks through the use of new genome technology



EWSMD

Establishment of an early warning system for mosquito -borne diseases



Emerging Viral Diseases-Expert Laboratory Network (Networking, rapid detection, training, EQAs)



ANTICIPATING EMERGING INFECTIOUS DISEASE EPIDEMICS



Anticipating emerging infectious disease epidemics: an informal consultation
1-2 December 2015, Geneva

drawn live
graphic recording | Drawing Change

following the International Health Regulations