FATAL HUMAN INFECTIONS WITH NEWCASTLE DISEASE VIRUSES

1. APMV-1 infections – a public health view

APMV-1 infections – a public health view

APMV-1 associated zoonotic risk early recognized:

virus isolation is rare

mild self-limiting disease usually reported: conjunctivitis + rarely flu-like ilness

no reports of human-to-human transmission

TABLE 2 | Cases of Avian Orthoavulavirus 1 virus infection in humans, confirmed by virus detection.

Year	Country	Patient details and known exposure/source	Symptoms	Outcome	Strain/genotype, accession number	References
1942	Australia	Laboratory worker, accidental exposure to cultured virus	Conjunctivitis, headache, chills	Recovered	Genotype unknown	Burnet (1943)
1946	Israel	23-year-old female Laboratory worker vaccinating chickens with cultured virus	Conjunctivitis with haemorrhage	Recovered	Genotype unknown	Shimkin (1946)
1945	Israel	Kitchen workers handling poultry, 3 males, 14 females, 13–70 years	Conjunctivitis	Recovered	Genotype unknown	Yatom (1946)
1946	Australia	Laboratory workers, accidental exposure to cultured virus; 2 cases	Conjunctivitis	Recovered	Same strain as 1942 case	Anderson (1946)
1947	USA	Veterinarian	Conjunctivitis	Recovered	Genotype unknown	Nelson et al. (1952)
1948	USA	Broiler plant operator and a veterinary student	Conjunctivitis, oedema of the eyelids, mucopurulent discharge	Recovered	Genotype unknown	Ingalls and Mahoney (1949)
1949	USA	Laboratory workers, accidental exposure to cultured virus; 3 cases	Conjunctivitis	Recovered	Genotype unknown	Freymann and Bang (1949)
1950	USA	Veterinarian performing diagnostic work	Conjunctivitis, headache, chills, malaise, periauricular lymphadenitis	Recovered	Genotype unknown	Gustafson and Moses (1951)
1951	USA	Volunteer/patient	Conjunctivitis, chills	Recovered	Beaudette strain Genotype II, virulent	Hunter et al. (1951)
1951	Canada	Laboratory worker, laboratory accident that aerosolized cultured virus	Flu-like illness	Recovered	Genotype unknown	Mitchell and Walker (1951)
1951	USA	Workers in a poultry processing plant, 40 cases	Conjunctivitis, oedema of the eyelids, adenitis	Recovered	Genotype unknown	Nelson et al. (1952)
1956	USA	Laboratory worker, accidental exposure to cultured virus	Conjunctivitis, crusted exudate, pain	Recovered	California 11,914 strain Genotype II, virulent	Reagan et al. (1956)
1960–1963	UK	Workers in two Broiler processing factories, 3 cases	Conjunctivitis	Recovered	Genotype unknown	Trott and Pilsworth (1965)
1962	USA	Aerosol exposure during vaccination of chickens	Bilateral conjunctivitis, headache, malaise, pharyngitis, fever; virus isolated from eyes and urine	Recovered	B1 strain Genotype II.II, avirulent	Dardiri et al. (1962)
1976	Malaysia	Female laboratory worker, accidental exposure to infected chicken organs	Conjunctivitis	Recovered	Genotype unknown	Mustaffa-Babjee et al. (1976)
2011	Pakistan	Poultry workers, 82 cases, 21–41 years old	No symptoms except for one person with mild respiratory symptoms	Recovered	MH019281 PK1 Genotype XIII.2.1	Shabbir et al. (2021)
2022	India	32-year-old male Painter, no known poultry contact	Keratoconjunctivitis, Co-infection with human adenovirus type 8	Recovered	Genotype unknown, no sequence available	Prajna et al. (2022)

Source: Abolnik, Hayes (2025) expanded from Ul-Rahman et al. (2021)
https://doi.org/10.1111/zph.70011, https://doi.org/10.1002/rmv.2246

APMV-1 infections – a public health view

APMV-1 associated zoonotic risk early recognized:

mostly occupational exposure

contact with infected birds / infectious biological material (including aerosols)

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APMV-1 infections – a public health view

APMV-1 associated zoonotic risk early recognized, however:

severe or fatal infections also reported (n = 7 published reports)

marked respiratory (pneumonia) symptoms + 2 cases of neurologic infection

immunocompromised patients or existing co-infections

Year	Country	Patient details and known exposure/source	Symptoms	Outcome	Strain/genotype, accession number	References
1953	USA	Patient 1: 37-year-old female; patient 2: 11-month-old female, virus also detected in the mother, family had contact with poultry; patient 3: 63-year-old male, immunocompromised with antecedent monocytic leukaemia	Fever vomiting, diarrhoea, bronchitis, convulsions, acute haemolytic anaemia. Virus isolated from blood over an extended period	Patients 1 and 2 recovered, patient 3 died	Genotype unknown	Moolten et al. (1953)
2003	Netherlands	54-year-old female, history of multiple myeloma Lived in a rural region near a city Immunocompromised, had received allogenic bone marrow transplant and immunosuppressive treatment Secondary infection with *Pseudomonas* spp.	Pneumonia	Died	hPPMV-1/ Netherlands/579/2003 KJ544861 Genotype VI.2.1.1.2.2[a]	Kuiken et al. (2018)
2007	USA	42-year-old male, history of non-Hodgkin's lymphoma. Urban dweller Immunocompromised, had undergone a peripheral blood stem cell transplant	Pneumonia	Died	Pigeon paramyxovirus EF555096 Genotype VI.2.1.1.1[a]	Goebel et al. (2007)
2021	China	64-year-old male, worked at a restaurant, handled and processed meat pigeons	Severe pneumonia	Died	Human/Shandong/2/2021 Bioproject PRJCA00635 #CRA004864 Genotype VI.2.1.1.2.2	Zou et al. (2022)
2021	France	12-year-old female, visited Dubai shortly before neurological symptoms started Immunocompromised, underwent haematopoietic stem-cell transplant	Meningoencephalitis, seizures, coma	Died	1902 M010210 avulavirus SAMN13611976 Genotype XXI.1.1[a]	Winter et al. (2021)
2022	Australia	2-year-old female, immunocompromised, infantile Pre-B cell acute lymphoblastic leukaemia	Upper respiratory tract symptoms, nausea, vomiting, fever, seizures	Died	Human/Australia/NSW/2022 OR636618 Genotype VI.2.1.1.2.2	Hurley et al. (2023)
2023	China	66-year-old male, history of hypertension, coronary heart disease, dyslipidemia Urban dweller, neighbour kept pigeons Post-COVID-19 syndrome (long COVID), SARS COV-2 coinfection	Fever, malaise, bronchitis, palpitations, abdominal pain, diarrhoea	Recovered	Human/Beijing/2023 Genotype VI.2.1.1.2.2	Cui et al. (2023)

Source: Abolnik, Hayes (2025) expanded from Ul-Rahman et al. (2021)
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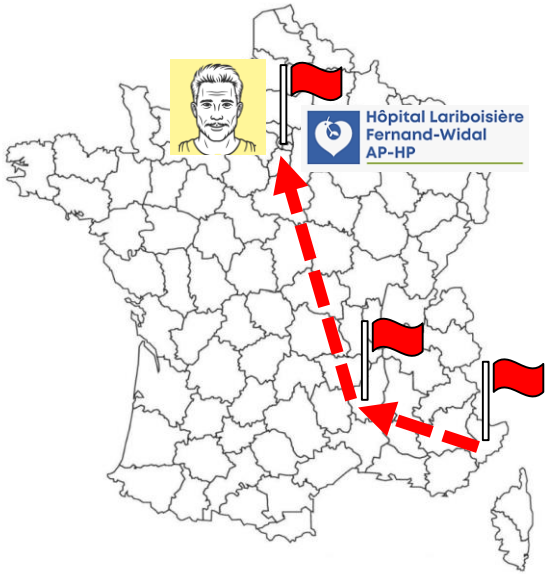
2. A recent French case of fatal encephalitis

case A – a retrospective investigation

(Veyrenche et al., submitted)

A recent French case of fatal encephalitis

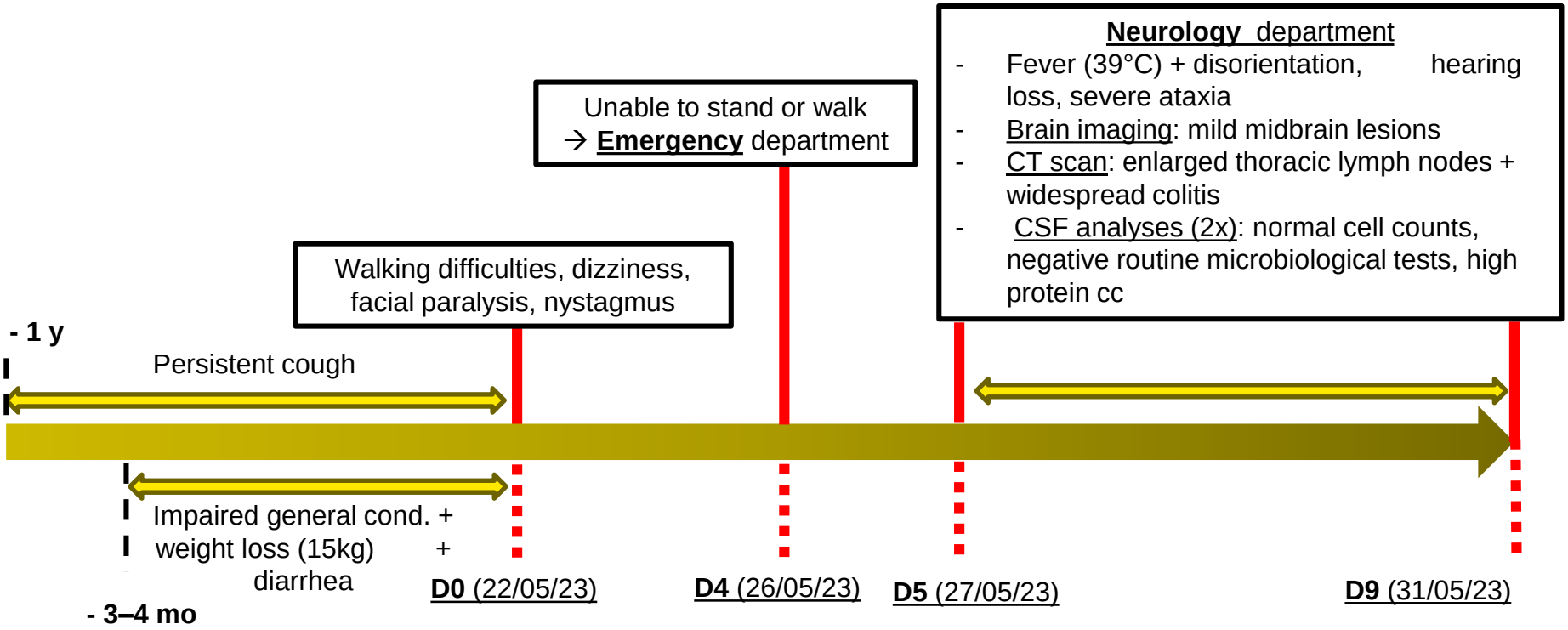
- 69-y-old male patient, no remarkable medical history and had not travelled outside continental France.
- **Impaired general condition** since 3-4 mo (weight loss 15 kg), **persistent cough** for 1 y + **episodes of diarrhea.**
- Admitted in hospital: had fallen at home, but still conscious.



<u>Case history – main timeline of events (10/05/23 – 20/06/23)</u>:

- 10/05 – 18/05: trip to SE France
- 18/05 – 24/05: shamanic workshop in S France (forest – Ardèche)
- 25/05: back home in Paris
- 26/05: admitted in **emergency** department, CHU Lariboisière
  27/05: **neurology** department, CHU Lariboisière
  01/06: **intensive care unit,** CHU Lariboisière
- 20/06: died from severe encephalitis and dysfunction of multiple peripheral nerves and spinal nerve roots.

A recent French case of fatal encephalitis



A recent French case of fatal encephalitis

Intensive care unit

Clinical presentation:

Coma + respiratory failure and aspiration pneumonia.
Deteriorated neurological examination: motor deficit (all 4 limbs).

Brain imaging: extensive diffuse cytotoxic edema

Metagenomic NGS on blood and CSF: negative

➔Severe encephalitis and polyradiculoneuropathy of unknown etiology

Patient died 26 days post-admission from worsening condition

D10 (01/06/23)

D29 (20/06/23)

A recent French case of fatal encephalitis

47 samples

5 peripheral and clinical samples

30/05/2023	sigmoid colon biopsy
01/06/2023	BALF
07/06/2023	CSF
07/06/2023	plasma
15/06/2023	whole blood

42 post-mortem tissues
(20/06/2023)

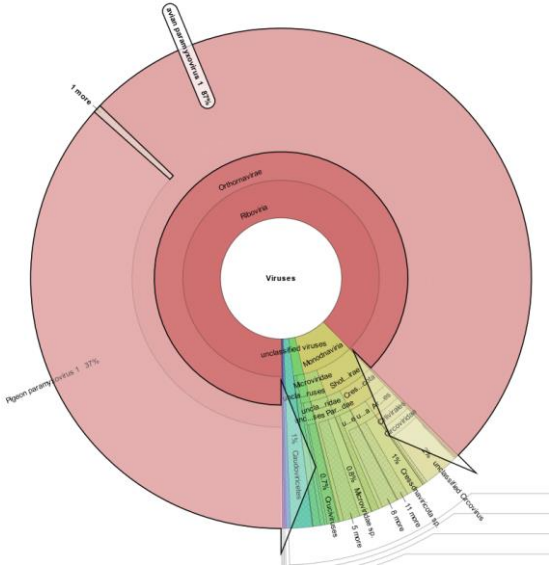
- **26 central nervous system** tissues:
→ **22** from the **Encephalon** + **4** from the **spinal cord**
- **2 thoracic spinal ganglions**
- **2 thoracic lymph nodes**
- **12 peripheral nerve** tissues

- 80 °C

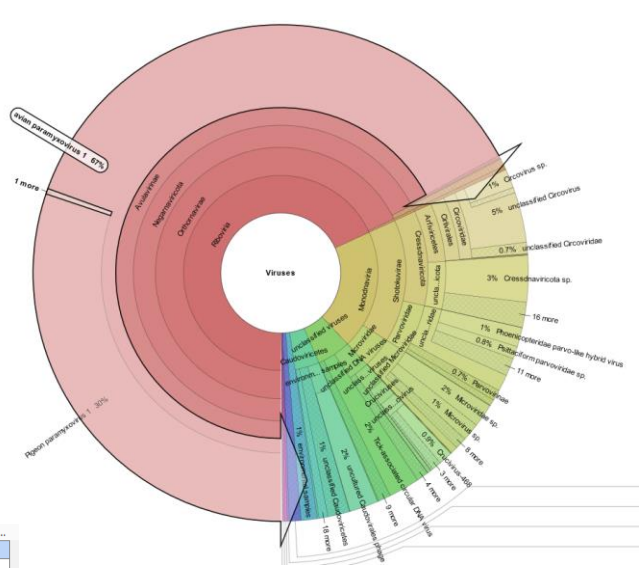
A recent French case of fatal encephalitis

mNGS

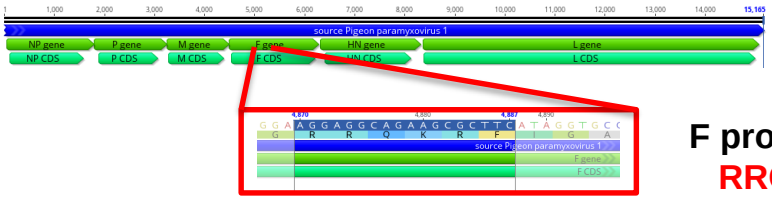
Midbrain PM tissue

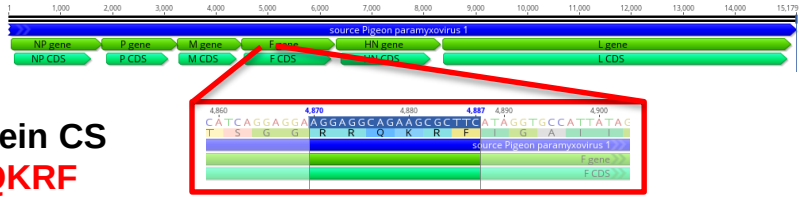


Cervical spinal cord PM tissue



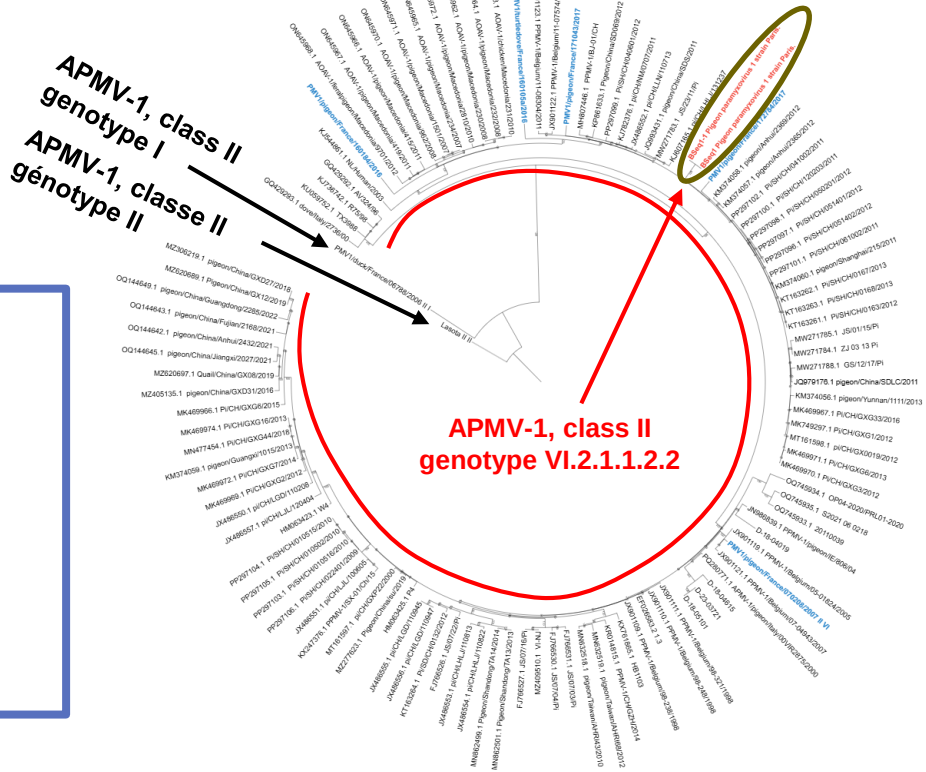
	NP24-0222...	NP24-0223...
NP24-0222-consensus-...		99.9%
NP24-0223-consensus-...	99.9%	





F protein CS
RRQKRF

A recent French case of fatal encephalitis



APMV-1, class II
genotype VI.2.1.1.2.2

97.64% nucleotide identity with Chinese sequence Pi/SH/CH/041002/2011

most closely related French sequence: 96.64% ident. pigeon/France/172784/2017 (dpt 31)

A recent French case of fatal encephalitis

in-house L gene-based APMV-1 specific rt RT-PCR

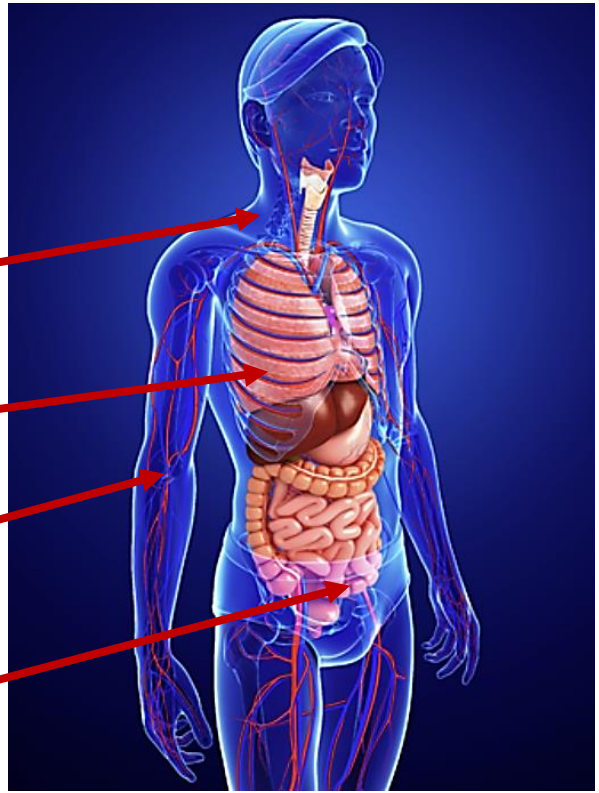
No APMV-1 genome detection

CSF

BALF

whole blood
plasma

sigmoid colon biopsy



A recent French case of fatal encephalitis

in-house L gene-based APMV-1 specific rt RT-PCR

Detection of APMV-1 genome (consistent with IHC staining of same tissues) **and trend towards later Ct values, from**

Forebrain/Midbrain/Hindbrain

to Spinal cord

and Thoracic spinal ganglions & lymph nodes

No APMV-1 genome detection in peripheral nerve tissues

Tissus post-mortem	RT-PCR (CT)
Biopsie temporale	15,38
cortex occipital (calcarine)	16,21
noyau caudé	16,25
noyau lenticulaire	16,82
thalamus	16,97
cortex temporal T1	17,33
gyrus cingulaire	17,96
cortex pariétal (GSM)	19,56
hippocampe	19,76
cervelet (ny dentelé)	21,33
noyau amygdalien	21,84
hypothalamus	23,63
cortex frontal F2	23,68
Biopsie mésencéphale	23,77
mésencéphale (substantia nigra)	24,05
cortex frontal supéro-interne	24,13
pont	25,63
moelle épinière cervicale	26,54
bulbe	27
corps calleux	27,1
substance blanche frontale	27,43
moelle spinale cervicale	27,81
moelle spinale lombaire	30,3
moelle spinale thoracique	31,51
plexus choroïde	32,2
hypophyse	33,85
ganglion rachidien thoracique bas	33,86
ganglion rachidien thoracique haut	35,98
ganglion lymphatique axillaire dt	36,06
ganglion lymphatique axillaire gch	36,92

Tissus post-mortem	RT-PCR (CT)
nerf ulnaire dt	Négatif
nerf ulnaire gch	Négatif
nerf axillaire dt	Négatif
nerf axillaire gch	Négatif
nerf radial dt	Négatif
nerf radial gch	Négatif
nerf médian dt	Négatif
nerf médian gch	Négatif
nerf sous-cutané (jambe) dt	Négatif
nerf sous-cutané (jambe) gch	Négatif
nerf sciatique bas / poplité dt	Négatif
nerf sciatique bas / poplité gch	Négatif

3. A summary of two other reported French APMV-1 human infection cases

Other reports of French APMV-1 human infection cases

Case B: a severe encephalitis in an immunocompromised patent (late 2024)

patient was exposed to pigeon droppings at home in France (+ exposed to falcons in bird markets in Morocco)

immunosuppression following treatment for hematologic disease

mNGS negative on CSF

mNGS on brain biopsy ➔ APMV-1 genotype VI.2.1.1.2.2

Case C: a fatal case of hepatitis & hemorragic syndrom

patient was admitted to hospital intensive care unit after returning from a trip to Saudi Arabia

clinical presentation: acute hepatitis + hemorragic syndrome ➔ suspicion of VHFs

late amplification in DENV-specific RT-PCR on urine + NS1 Ag detection in blood

mNGS on plasma and post-mortem liver tissue ➔ APMV-1 genotype VI.2.1.2

APMV-1 genome detection by specific rt RT-PCR on the same previous samples

+ 3 other ante-mortem samples (sputum, urine and CSF)

4. Conclusion

Conclusions

APMV-1 infection should be considered for patients presenting with encephalitis or pneumonia of unknown etiology,

even when there is no indication of immunosuppression or
when no obvious exposure to potentially infected birds is present.

Importance of mNGS strategy to elucidate the 3 reported APMV-1 human infection cases (rare and difficult differential diagnosis).

Choice of samples may be crucial: detection in CSF is not constant

➔ lymph nodes could be a less invasive option than brain biopsies.

Increased frequency of immunosuppression is likely to occur, given the improvement and availability of new cancer treatments

➔ relevant information should be provided to patients to help them avoid at risk exposure.

Acknowledgements :

Anses NGS platform VIRPIG unit

Aurélie Leroux, Yannick Blanchard

French national reference laboratory for Newcastle disease VIPAC unit

Éric Niqueux, Béatrice Grasland, François-Xavier Briand, Audrey Schmitz

Assistance publique – Hôpitaux de Paris

Nicolas Veyrenche, Susana Boluda, Marianne Leruez-Ville, Anne Jamet, Agnès Ferroni, Maud Salmona, Linda Feghoul, Isabelle Plu, Jacques Fourgeaud

Jérôme Le Goff, Séverine Mercier Delarue, Marie Jaspard

Théodore Soulier, Sophie Demeret, Nicolas Weiss, Loïc Le Guennec, Adam Celier, Pierre Cappy

Hôpital Lariboisière – INSERM

Isabelle Malissin, Bruno Megarbane

Institut Pasteur

Philippe Pérot, Béatrice Regnault, Laurine Robert-Capraro, Nolwenn M Dheilly