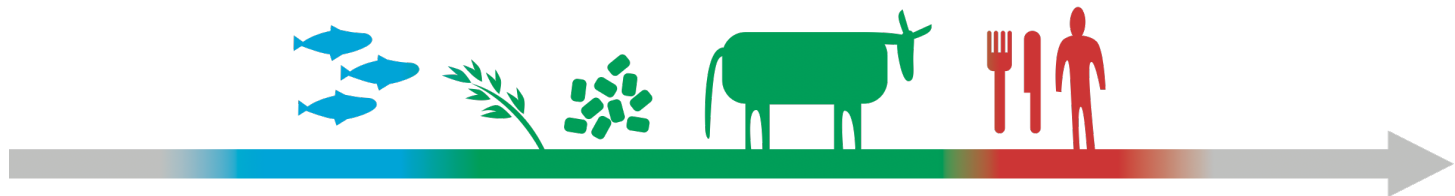




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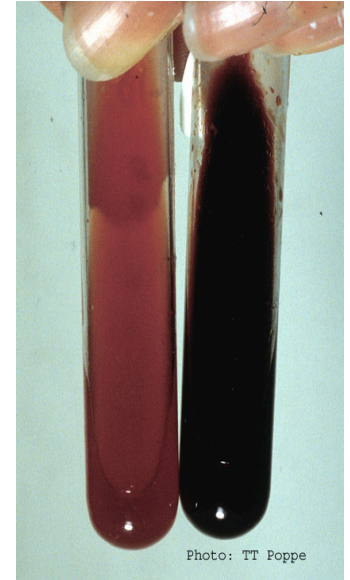
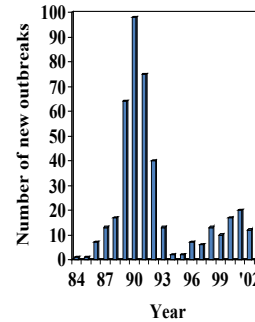
# Clinical and histopathological characterization of ISA outbreaks in Norway in 2020

*Ole Bendik Dale - Geir Bornø*  
*Norwegian Veterinary Institute*



# Infectious salmon anemia - short history

- 1<sup>st</sup> detected in Norway 1984
- Listed disease - EU / OIE
- Disease affect farmed Atlantic salmon
- The causative orthomyxovirus primarily induce a severe anemia with consequences
- Traditional biosecurity work well but normal, wild-type HPRO may (re-)emerge as virulent HPRdel



# Gill HPR0

->

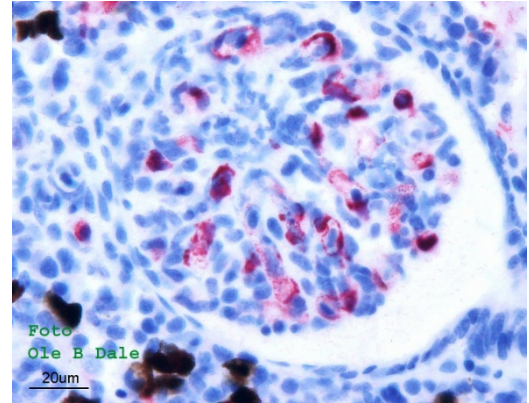
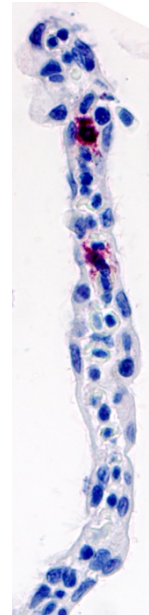
# Organ HPRdel

ISAV-HPR0 a waterborne infection of external epithelium, no clinical disease, virus sheds back to the water

Virulent HPRdel ILAV - infect endothelial cells on the inside of blood vessel and virus is shed to the blood



How?



Gill

Gill

Kidney

# ISAV receptor distribution in organs: cardiovascular endothelium + RBC

ISA-virus used as a probe

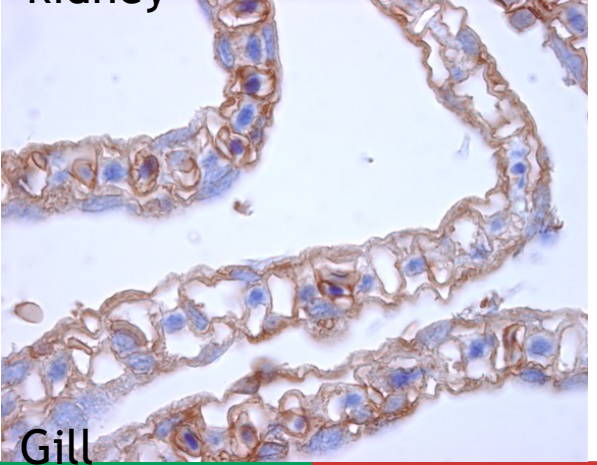
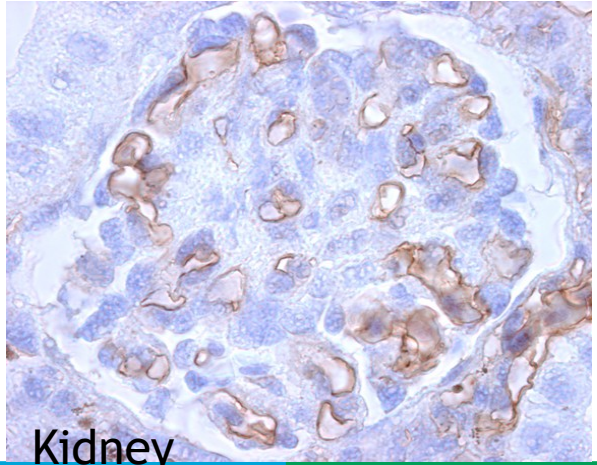
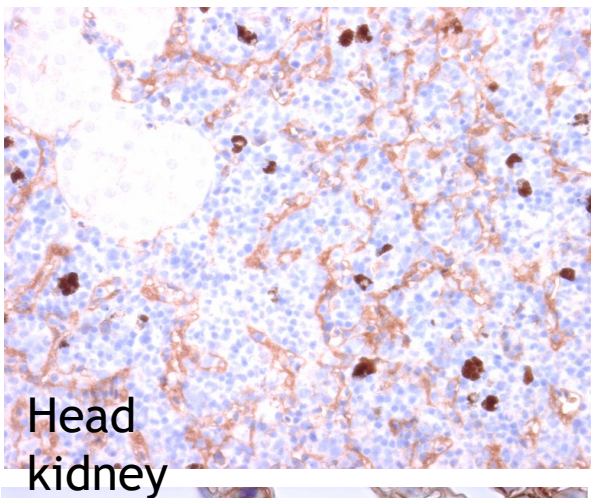
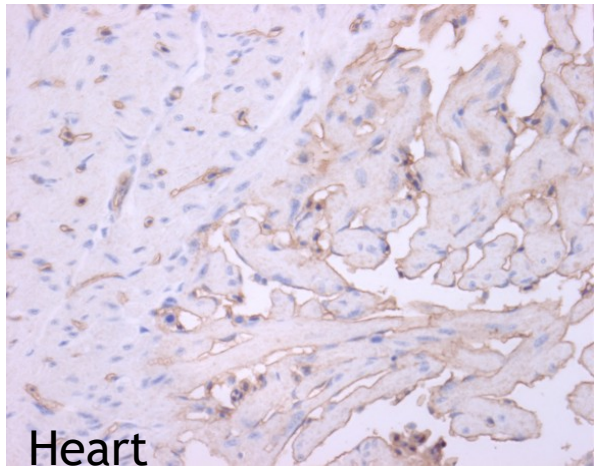
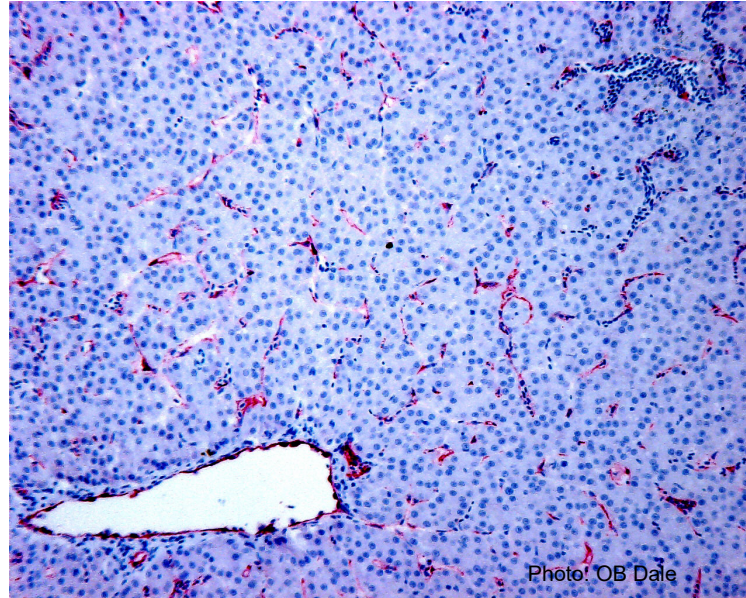


Photo:  
Maria Aamelfot



# Systemic HPRdel ISA-virus infection is governed by receptor presence, i.e blood vessels:

No vasculitis  
nor local spread  
outside vessels

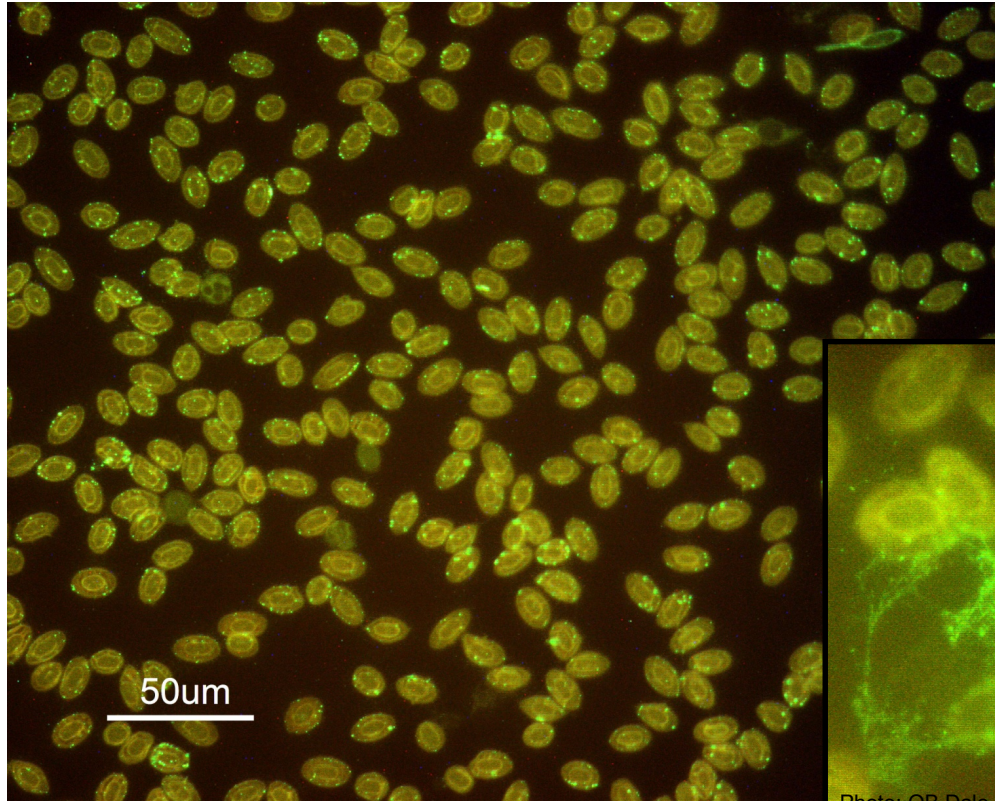


Virus is shed  
into the vessel lumen  
and then what:

# Virus attach (for too long) to Red Blood Cell (RBC) surface: may induce hemagglutination and erythrophagocytosis

Fluorescent stain  
using Mab detecting  
ISAV HE-protein:

Bright green  
dots are marking  
virus proteins  
on RBC surface



Insert:  
macrophage in action

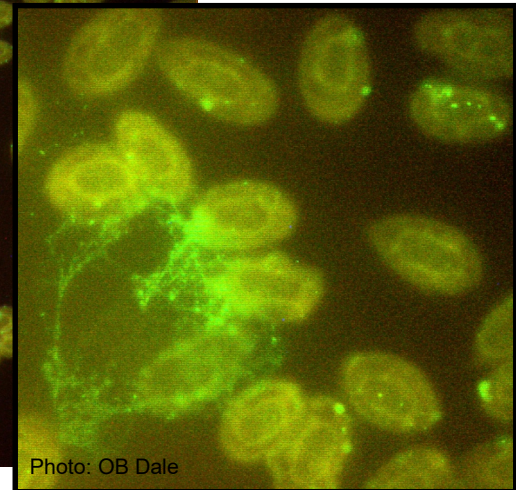
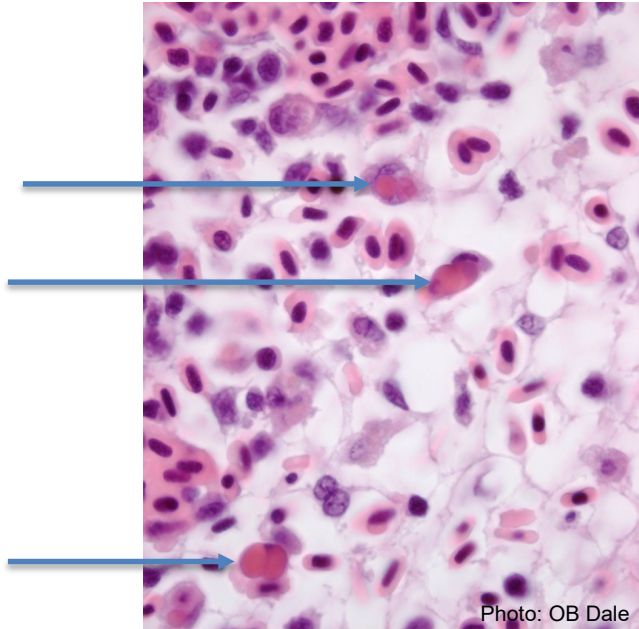


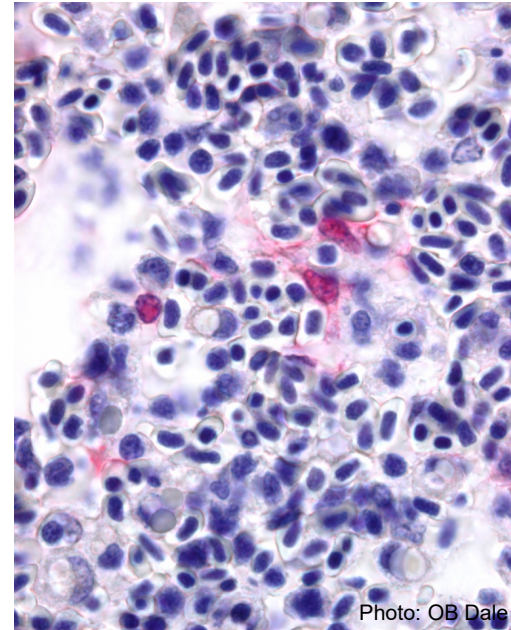
Photo: OB Dale



# Anemia: Increased erythrophagocytosis in spleen

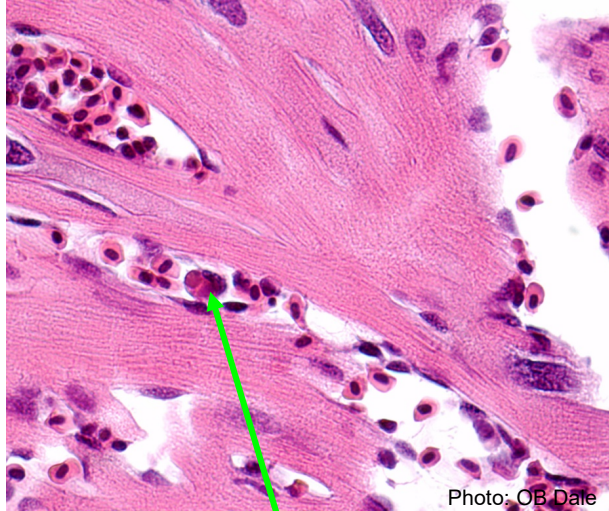


HE-stain

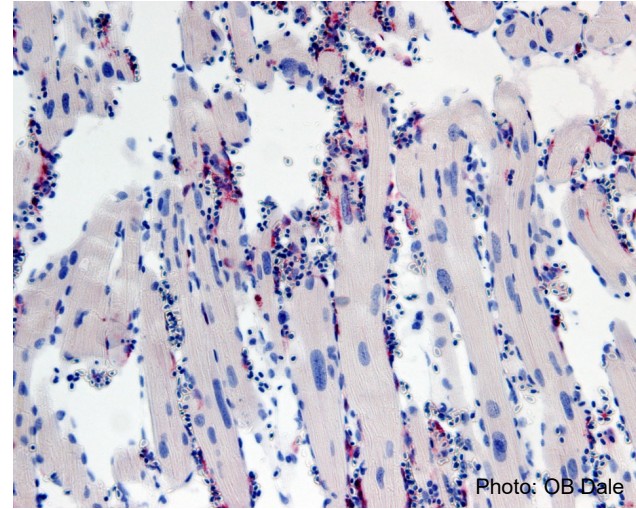


Immunohistochemistry  
detecting ISAV nucleoprotein

# Erythrophagocytosis also in organs other than spleen



Heart HE-stain:  
erythrophagocytosis



Heart IHC: extensive  
endothelial infection



# Endstage pathology: Classical ISA

**Always:** ascites / edemas / enlarged spleen

**Variable;** Hemorrhages

- Hemorrhagic liver necrosis
- Hemorrhagic kidney syndrome (HKS)
- Hemorrhagic gastrointestinal wall
- Other, e.g. anterior eye chamber

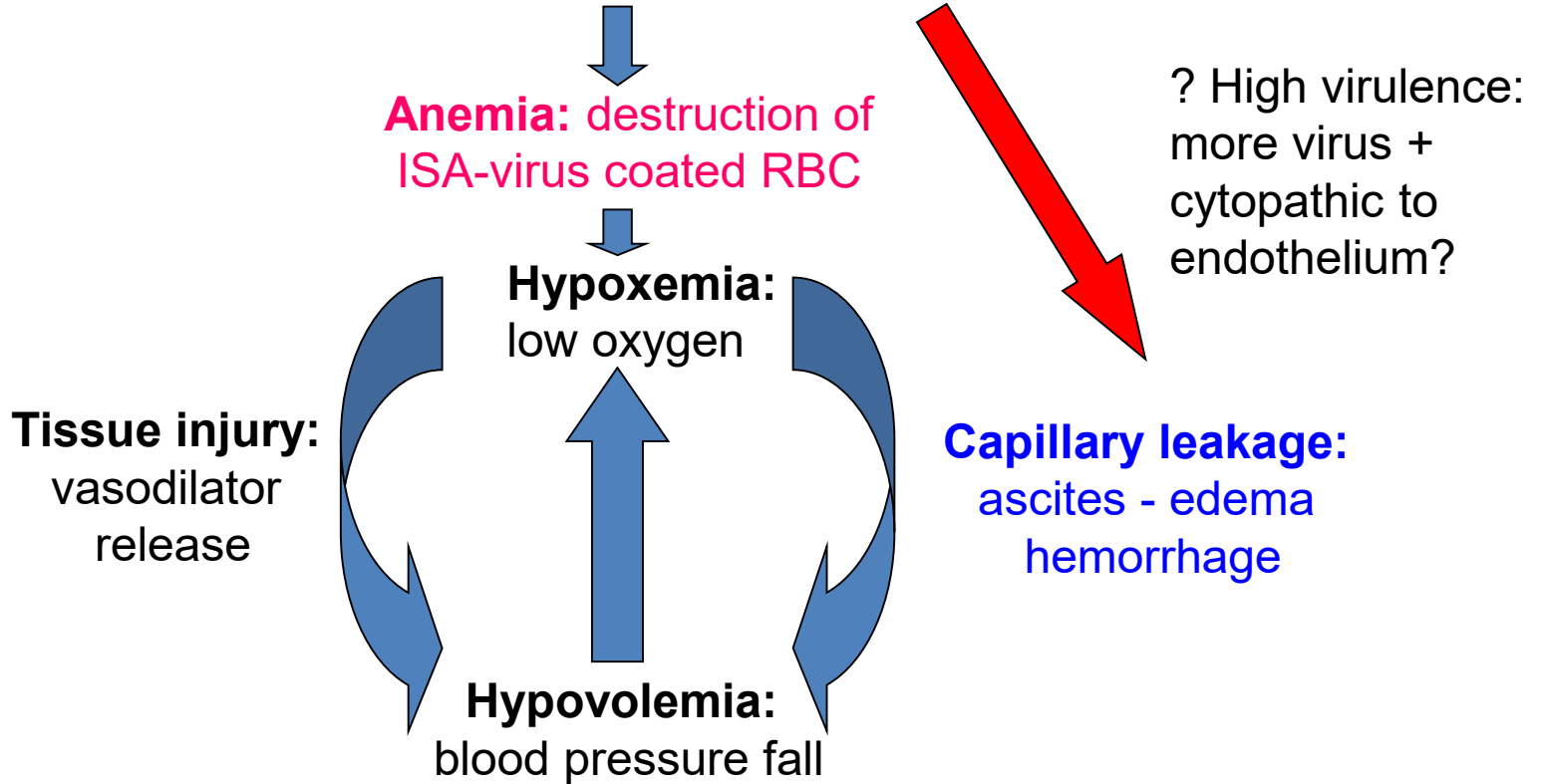
One hemorrhagic manifestation  
may dominate in an outbreak

or

Several manifestations together -  
even in the same fish



# ISA-virus infection of blood vessel endothelium



**Vicious circle: Shock >>> Death**

# ISA may now hide among many health problems!

## Detections in 3 main contexts:

### 1. PCR screening in the industry

- most often low prevalence and high Ct values, no ISA disease outbreak - no apparent anemia, but HPRdeleted found
- in few cases: low Ct values and RBC breakdown apparent, IHC show widespread infection

### 2. Epidemiological links to known cases

- traditional tracing
- «new»: outbreaks in early seawater phase - links to hatcheries

### 3. Routine disease diagnostics

- often no suspicion of ISA before histopathology show circulatory disturbances / increased RBC breakdown and a specific test is done to be «on the safe side»
- other diseases concurrently in the farm

# Clinical pathology - disease changes ?

## Before:

1. Low, elevated daily, persistent mortality up to ~ 0.05%
2. No or slow disease spread from net-pen to net-pen
3. Seasonality, disease outbreaks mid - winter/summer
4. The outbreak never stops: high cumulative loss
5. Moribund fish in normal nutritional condition with hematocrit close to zero
6. Episodes of very high, acute mortality: induced by stressing severely anemic fish?

## Now:

1. **Unchanged, but obscured by more «background» mortality?**
2. **Unchanged**
3. **Seasonality still relevant, but PCR screening may detect the infection before disease becomes obvious**
4. **Outbreaks are stopped by control measures**
5. **Not common now - a feature of overlooked cases (but Hct not measured these days...)**
6. **Not common now - a feature of overlooked cases**

# Recent case - no suspicion before histopath...

**Main disease finding:** septicaemia and deep skin wounds due to *Moritella viscosa* / *Vibrio wodanis*.

Histopath **other** findings:

- Kidney; hemorrhages / congestions
- Liver; minor degenerative/necrotic changes, vacuolization hepatocytes, congestion
- Spleen; major circulatory disturbances
- Pyloric ceca; minor congestion

No «classical ISA», but difficult to rule out ISA: test!

So far most such cases are false alarms - but not this one

Spleen, HE-stain  
major circulatory  
disturbances

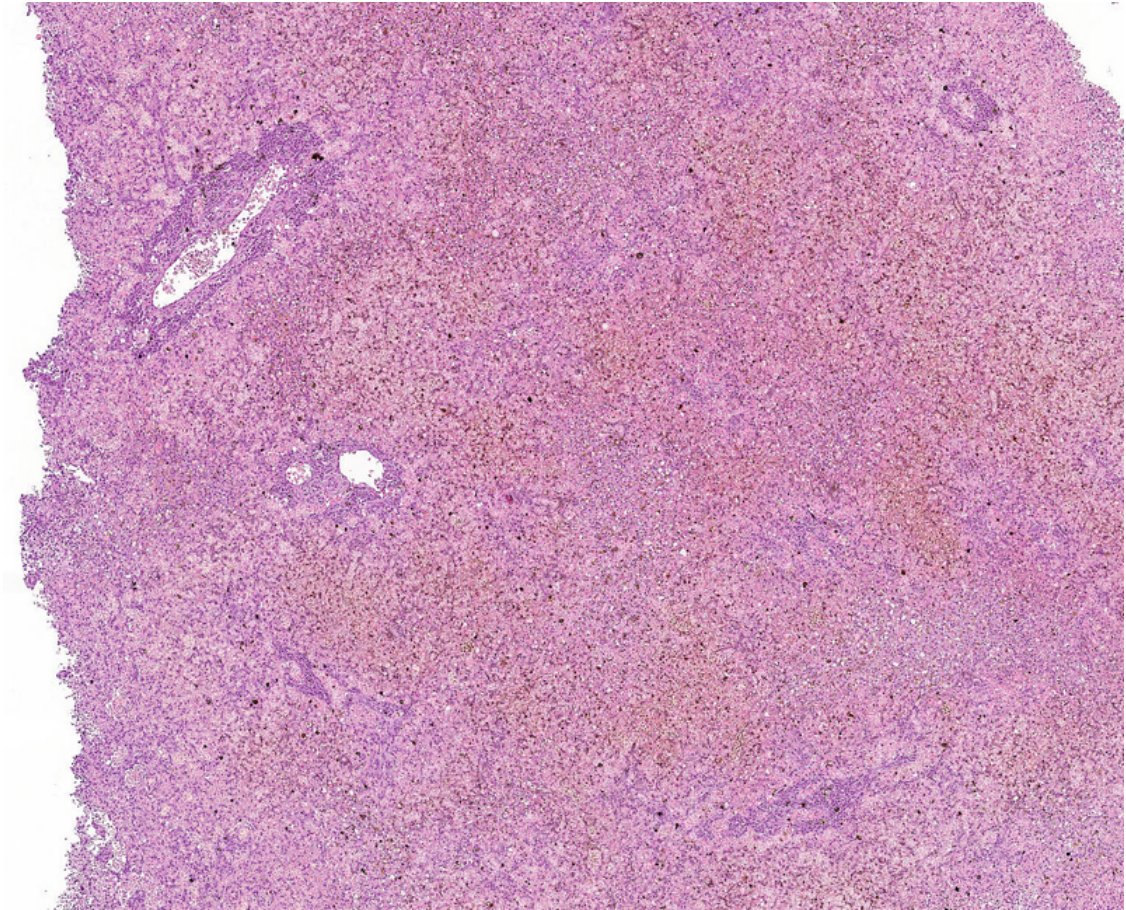
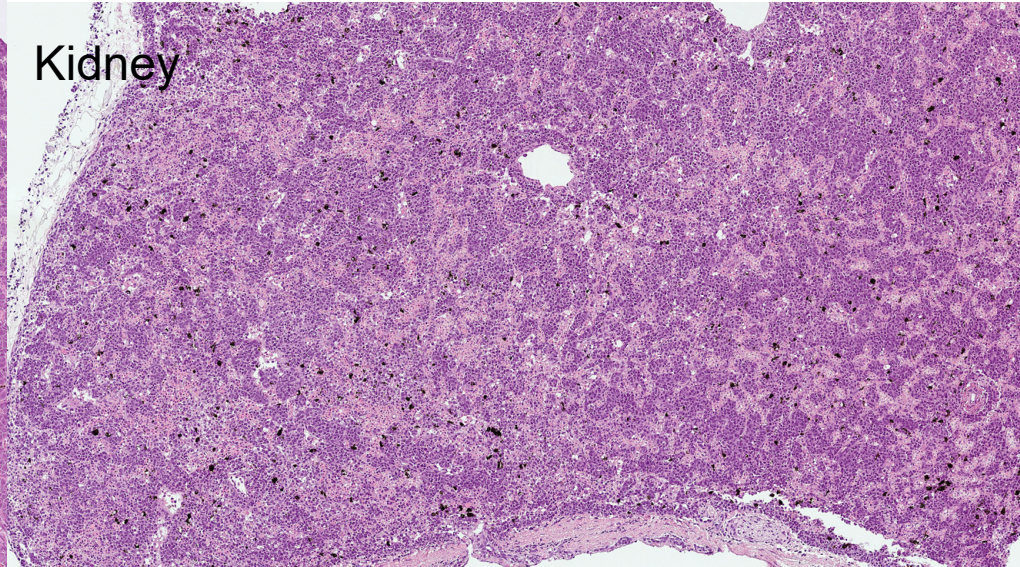
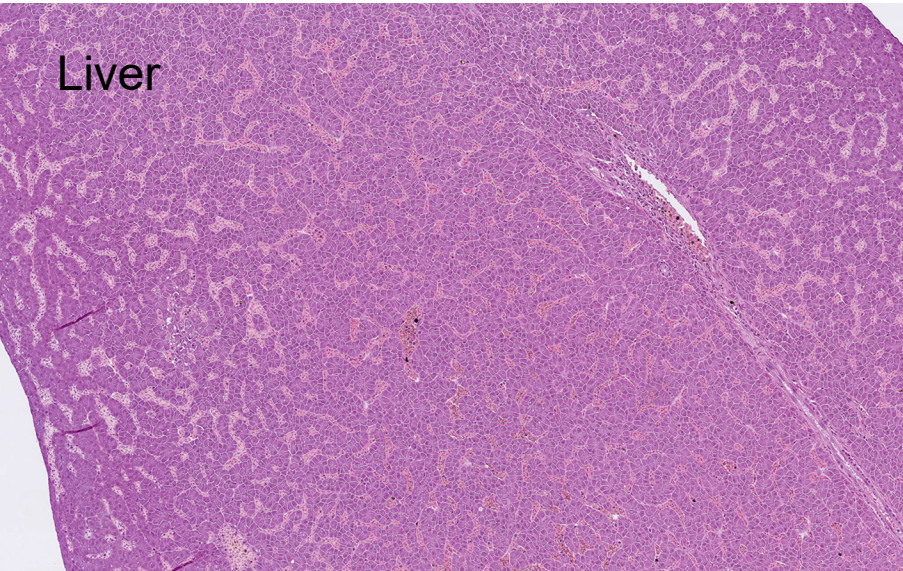


Foto: Lisa Furnesvik

Pattern on HE-stain:  
liver/kidney sinusoides dilated  
and filled with RBC: time to test



Thanks to all good colleagues at NVI and elsewhere

– past and present!



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