Bad Blood? An Evolving Tale of Risk Within a COVID-19 World

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EBF 13th Open Symposium 2020

Science
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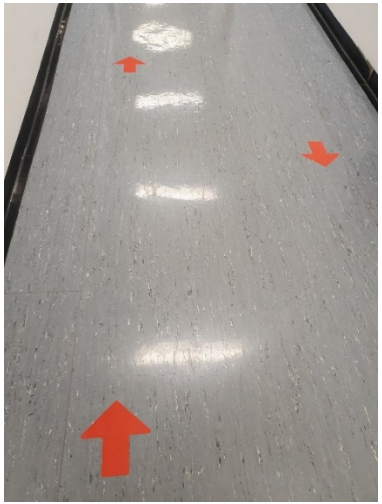
The difference a year makes

The need for personal space:

- Split shifts
- Working From Home
  - > Enabling remote access
  - > IT requirements & equipment

Keeping clean:

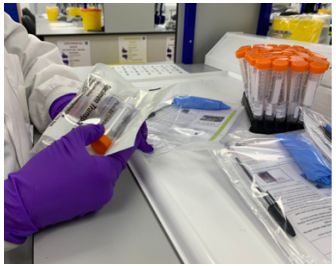
- Change in cleaning rotas
- Fire door access
- Providing hand wash/sanitiser stations
  - > Making hand sanitiser

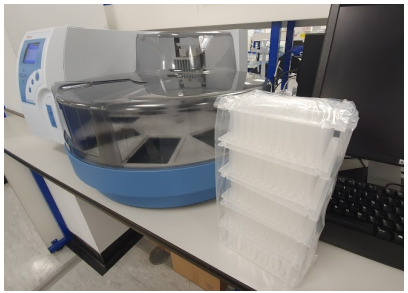


Microbiology safety cabinets

As the pandemic evolved

- Diversified the work we do (kit building/bio-banking)
- Heightened awareness of product shortages & increased communication with suppliers
- Remote QA auditing
- Patient centric sampling drive – COVID and beyond…
- Forced us to do things differently - not necessarily a bad thing (more efficient? more effective?)





Risk Assessment stage 1: The beginning

- Require notification of *potential* COVID samples
  - > BBV sample handling approach – limited capacity
- Extrapolating knowledge from SARS/MERS [1,2]
  - > Matrix prevalence of vRNA
  - > Virus Deactivation
  - > Medical evidence on exposure risk from SARS/MERS samples?
- No data ≠ No risk

"this is a respiratory disease - blood samples are less dangerous than the person in the hood next to you."

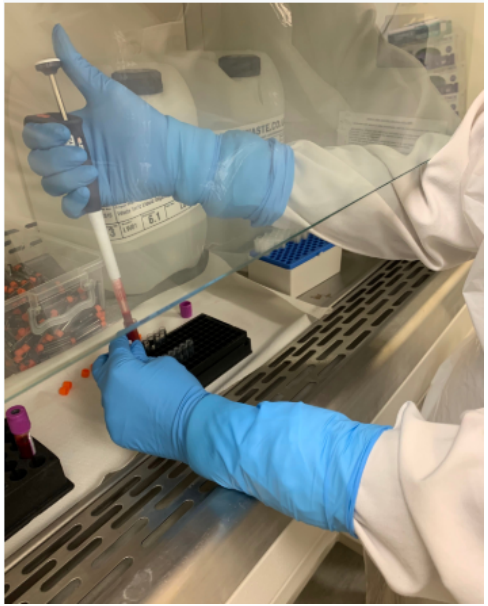
1) Darnell & Taylor "Evaluation of inactivation methods for severe acute respiratory syndrome coronavirus in noncellular blood products" Transfusion 2006, 46(10):1770-7
2) Darnell, Miriam E R et al. "Inactivation of the coronavirus that induces severe acute respiratory syndrome, SARS-CoV." Journal of virological methods vol. 121,1 (2004): 85-91

Stage 1

All suspected COVID samples handled in MSC hood until deactivation

> LC-MS = protein denaturation stage

> Early reports for heat deactivation used 60°C [1]
- impact on a number of biologics



Islands of automation?

> Need to build more hoods?

> Power, gas lines etc in the hood

1) Kampf G, Voss A, Scheithauer S. Inactivation of coronaviruses by heat. *J Hosp Infect*. 2020;105(2):348-349.

Stage 2: Government Guidance – Public Health England

Update on 28th March 2020

Guidance

COVID-19: safe handling and processing for samples in laboratories

"Exposure to upper and lower *respiratory tract specimens* in the absence of appropriate containment and control measures is likely to represent the *greatest risk* of SARS-CoV-2 laboratory acquired infection."

Stratify samples by Risk:

Respiratory tract samples > Faeces/Urine > Blood/Serum/Plasma

"Clinical laboratories must perform their own risk assessments for handling biological specimens from patients with suspected or confirmed COVID-19"

Advice from NHS trusts

CL2 - “diagnostic assays using whole blood, serum and plasma, including routine biochemistry and haematology, unless there is a risk of generating aerosols”

Specialist clinical chemistry facilities (LCMS, ELISA etc) vs bioanalytical labs?

High Risk - respiratory tract specimens, faeces

Low Risk – urine, blood, serum, plasma, CSF

The biggest risk is still other people – distance, wash hands, don’t touch your face

Handling SARS-CoV-2 +ve blood:
Focus on the greatest area of risk

Categorise staff risk –high risk, moderate risk etc

Evidence in the literature

RT-PCR on samples from 205 patients:

BALF (93%), sputum (72%), nasal swabs (63%), fibrobronchoscope brush biopsy (46%), pharyngeal swabs (32%), feces (29%), and blood (1%). None of the 72 urine specimens tested positive [1]

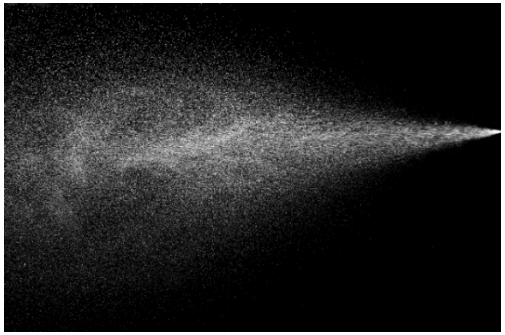
Infectious virus was readily isolated from samples derived from the throat or lung, but not from stool samples—in spite of high concentrations of virus RNA. Blood and urine samples never yielded virus (9 cases) [2]

1) Wang, Xu etal “Detection of SARS-CoV-2 in different types of clinical specimens” JAMA 2020 March 323(18):1843-1844
2) Wolfel, Corman etal “Virological assessment of hospitalized patients with COVID-2019” Nature 2020 May 581(7809):465-469

Stage 2 - Aerosol production & blood samples

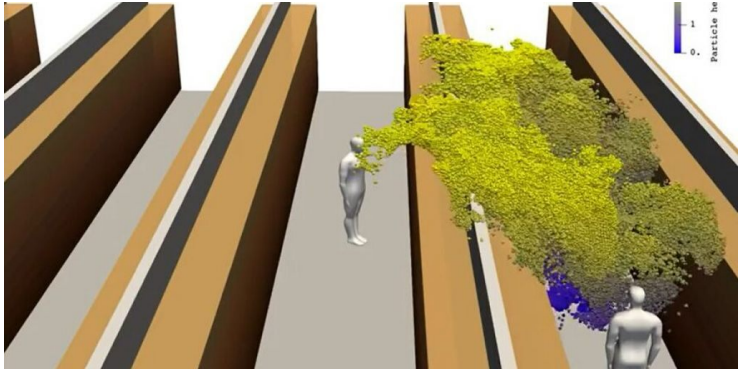
Processes with higher risk

- Centrifuge buckets,
- Liquid handlers,
- Vortexing



Assess each workflow & minimise aerosol risk or investigate deactivating the samples

Shouldn’t we always be concerned about aerosol production?



Deactivation data

SARS-CoV-2 can be deactivated with [1]

- TRIzol
- Formaldehyde
- beta-propiolactone
- 100°C for 5minutes
- 56°C for 45minutes

Impact on Biologics/Serology/Biomarkers

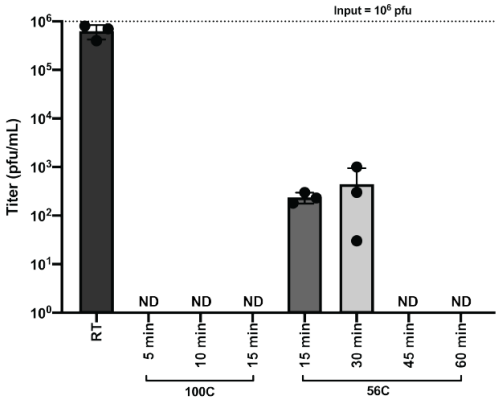


Figure 5. Heat Inactivation of SARS-CoV-2. SARS-CoV-2 containing samples (1x10⁶ pfu) were heated at 100C for 5, 10 and 15 minutes and 56C for 15, 30, 45, and 60 minutes. Samples were assayed by plaque assay to detect remaining infectious virus post-heating. The room temperature control was incubated at room temperature until all heated samples were prepared. Data are representative of the mean and SEM of 3 replicates.

1) Jureka, A.S.; Silvas, J.A.; Basler, C.F. Propagation, Inactivation, and Safety Testing of SARS-CoV-2. *Viruses* **2020**, *12*, 622

Stratifying by Sample Type

Guidance
COVID-19: safe handling and processing for samples in laboratories

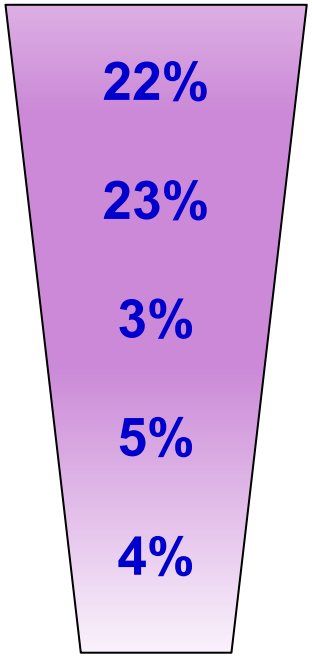
Confirmed COVID samples

High Risk
- Cleaning Initial samples during unpacking
- Respiratory samples (Nasal swabs, BALF, sputum)
- Faeces
- Urine
- Plasma/Serum/Blood where risk of Aerosol production

Low Risk
- Deactivated samples
- Plasma/Serum/Blood where no risk of Aerosol production
- Dried blood samples
- Dried blood eluates containing Tween

Stage 3 – Further data comes to light

Hospital staff prevalence – June/July 2020 (>4000 staff)



Ambulance/Paramedics

COVID wards, Phlebotomists, Triaging

Non-COVID ward staff

GP staff

Pathology Laboratory staff

Stage 3 – New reports in the literature[1]

RT-PCR on plasma/serum samples from 674 acute and convalescent cases & attempted virus isolation from a subset of RNA-positive samples.

vRNA - 12.7% of COVID patient serum samples (n=212) & 0% ≥28 days post symptom onset (n=494)

RT-PCR Cycle threshold was high (range 33.5-44.8) – low copy numbers?

PCR-positive sera inoculated into cell culture did not produce any cytopathic effect or yield an increase in detectable SARS-CoV-2 RNA.

1) Andersson MI, Arancibia-Carcamo CV, Auckland K et al. SARS-CoV-2 RNA detected in blood products from patients with COVID-19 is not associated with infectious virus. Wellcome Open Res 2020, 5:181

“vRNA was detectable at low viral loads in a minority of serum samples collected in acute infection, but was not associated with infectious SARS-CoV-2 (within the limitations of the assays used). This work helps to inform biosafety precautions for handling blood products from patients with current or previous COVID-19."

1) Andersson MI, Arancibia-Carcamo CV, Auckland K et al. SARS-CoV-2 RNA detected in blood products from patients with COVID-19 is not associated with infectious virus. Wellcome Open Res 2020, 5:181

Bad Blood?

No change for high risk samples

All COVID confirmed primary tubes handled & cleaned in MSC

Plasma/Serum/Blood at CL2*

Education & Training

Remain vigilant to our PPE procedures when handling samples

Thank you

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