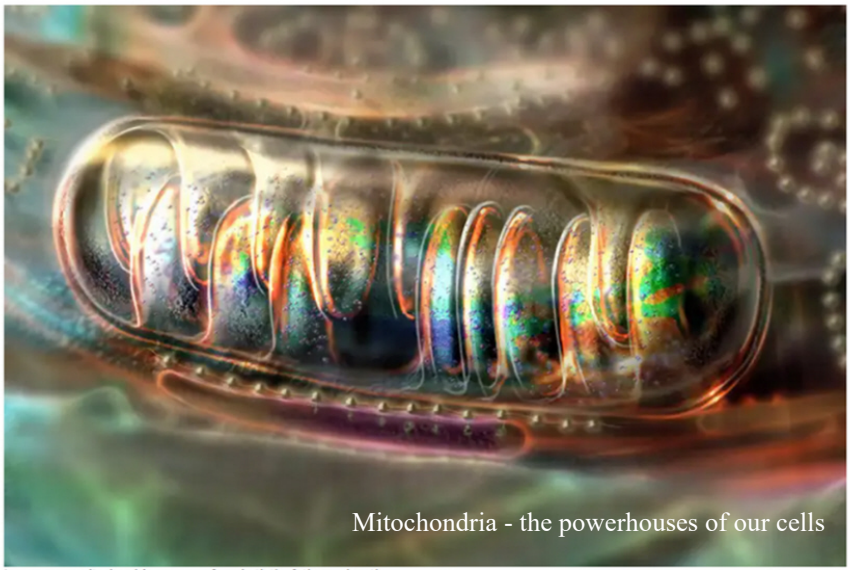
Creating international and interdisciplinary collaboration for health

AONM Newsletter January 2022



Mitochondria - the powerhouses of our cells

As AONM's first newsletter of the year we wish you all a far brighter 2022; hopefully this world will soon be in a better place.

This newsletter features an article on Long Covid, touching on recent findings about the driving pathways of the condition. We also introduce some exciting new tests that AONM has recently brought over from Germany: mitochondrial tests using extracellular flux analysis with luciferase assays and the Seahorse XF system. The Seahorse has evolved into a leading-edge system for mitochondrial testing, and is regularly used in studies across the world.

AONM longs to be able to start organising in-person meetings and conferences again. We are not sure we are quite there yet, but until then we will be running a further series of webinars: please see our Events section, and watch this space.

CONTENTS

1. The devastation of CD16+ monocytes in Long-COVID

The University of Washington in Seattle reported that almost a third of those who have been infected with COVID suffer from persistent symptoms nine months later – a condition that has come to be called Long-COVID, long-haul syndrome or PASC (post-acute sequelae of COVID-19).(i)

Persistence of the spike protein in monocytes for 15 months

The underlying mechanisms of Long-COVID have long been opaque, but an October 2021 study by Bruce Patterson et al entitled "Persistence of SARS CoV-2 S1

©2022 Academy of Nutritional Medicine (AONM)

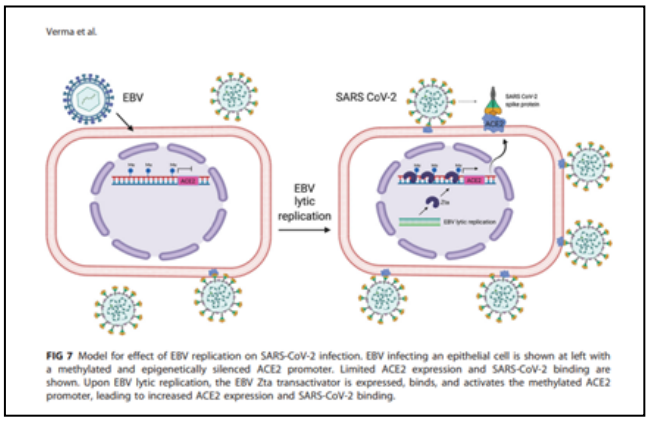
Protein in CD16+ Monocytes in Post-Acute Sequelae of COVID-19 (PASC) Up to 15 Months Post-Infection" found that the S1 segment of the spike protein is recoverable from human monocytes in PASC patients up to 15 months after their acute infection, compared to controls.(ii) As board-certified internist and cardiologist Dr. Peter McCullough explained in a recent interview: "This means the body has literally been sprayed with the virus and it spends 15 months, in a sense, trying to clean out the spike protein from our tissues. No wonder people have Long-COVID syndrome."(iii)

What might the SARS-CoV-2 spike protein in these intermediate and non-classical monocytes be doing? Patterson et al describe high IFN-γ levels in PASC individuals, which can induce TNF-α production, both highly pro-inflammatory cytokines. "Manifestation of the senescence-associated secretory phenotype (SASP)" is described in the same study, characterized by high basal NF-κB activity and production of other pro-inflammatory cytokines such as IL-1α and IL-8. The production of these cytokines drives "the permanency of S1-containing cells in the circulation." The Spike protein is well researched already as causing huge inflammation, and these "spiked" monocytes appear particularly apt to cause inflammation in vascular endothelial cells.

CD16+ monocytes (as featured in the title of the paper) have previously been demonstrated to migrate into the brains of AIDS patients and mediate blood-brain barrier damage and neuronal injury via their release of proinflammatory cytokines and neurotoxic factors, the paper describes. "These sequelae are very common in PASC and these data could represent the underlying mechanism for the symptoms." Another point that the study highlights is that a number of papers have discussed the increased mobilization of CD16+ monocytes with exercise. "These data support the reports of worsening PASC symptoms in individuals resuming pre-COVID exercise regimens".

Reactivation of viral loads

These monocytes able to acquire such a proinflammatory phenotype can also act as a viral protein reservoir. "The significance of these cells as a viral protein reservoir in PASC is supported by our data reporting the presence of S1 protein within nonclassical monocytes." This accords with the finding that previous viral loads appear to reactivate with COVID-19 in some cases.(iv) A study in "Pathogens" in June 2021 reported: "These findings suggest that many Long-COVID symptoms may not be a direct results of the SARS-CoV-2 virus but may be the result of COVID-19 inflammation-induced EBV reactivation."(v) The findings of the study "Positive Epstein-Barr virus detection in coronavirus disease 2019 (COVID-19) patients" were similar.(vi) And equally a previous herpes virus load appears to provide fertile soil for SARS-CoV-2. The article "Epstein-Barr Virus Lytic Replication Induces ACE2 Expression and Enhances SARS-CoV-2 Pseudotyped Virus Entry in Epithelial Cells"(vii) describes this phenomenon. The figure below from that article shows the model by which "EBV infection and entry into lytic replication may induce ACE2 expression and enhance SARS-CoV-2 susceptibility in human oral epithelium."



Journal of Virology

Hijacking and reprogramming of the mitochondria

The mitochondrial impact of SARS-CoV-2/COVID-19 was covered in the last AONM newsletter (https://aonm.org/wp-content/uploads/2021/09/AONM-Newsletter-September-2021.pdf), and is doubtless a huge driver in Long-COVID presentations. Numerous articles have now described how SARS-CoV-2's RNA localises to mitochondria and "hijacks the host cell's mitochondrial function to viral advantage."(viii) The "markedly reduced aerobic capacity" of Long-COVID patients is bound to be in large part due to the mitochondrial impairment that results. A very recent study (January 2022) by Ajaz et al revealed the extensive mitochondrial reprogramming in PBMCs (peripheral blood mononuclear cells) of patients with COVID-19 to the benefit of the virus using Seahorse XF technology.(ix)

The remarkably wide range of persistent or recurrent symptoms reported by individuals following SARS-CoV-2 infection includes the following:

- severe fatigue
- reduced exercise capacity
- breathlessness
- chest pain or heaviness
- fever
- palpitations
- cognitive impairment – "brain fog"
- anosmia or ageusia
- vertigo and tinnitus
- headache
- peripheral neuropathy
- metallic or bitter taste
- skin rash
- joint pain or swelling

Table 1

Disordered iron metabolism

The disordered iron metabolism identified from the outset and the resulting hyperferritaemia (over 400 scientific articles on this linked to COVID-19 have already appeared) will be a major player, too, linked inevitably to assault of reactive oxygen species (ROS), further inflammation, and the concomitant hypercoagulability– reasons why testing for ferritin, D-Dimer and fibrinogen (amongst multiple other markers) is often so highly indicated.

Overlaps with M.E.

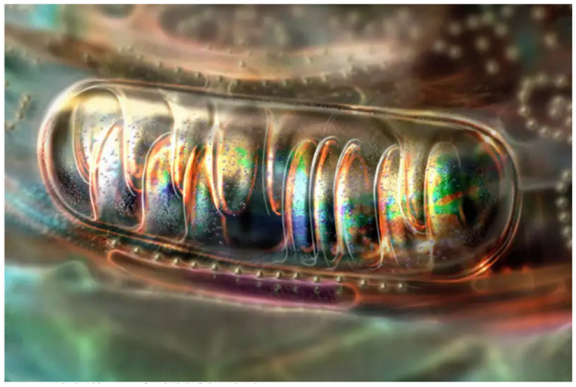
The Royal Society's SET-C (Science in Emergencies Tasking: COVID-19) group in their report "Long Covid: What is it and what is needed?" describe the wide range of symptoms reported by individuals following SARSCoV-2 infection(x) *(see Table 1 above)*:

Some characteristics of Long-COVID overlap with those M.E., especially if one also considers the blood-brain barrier incursion and neuronal injury identified for the CD16+ cells. The neurotoxicity of the latter has been well described both in this new and in previous studies. With the neurological disruption and the pain that can cause, one wonders whether metabolic similarities may yet be discovered if and when corresponding studies are undertaken on patients with M.E.

"Long COVID Day" organised by Biolab Medical Unit will be taking place on 25th March 2022: please see "Upcoming events" for further details.

i. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776560
ii. https://www.biorxiv.org/content/10.1101/2021.06.25.449905v1
iii. https://www.youtube.com/watch?v=3AgvHVOo2Hg
iv. https://journals.asm.org/doi/pdf/10.1128/JVI.00192-21
v. https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC8233978/
vi. https://www.nature.com/articles/s41598-021-90351-y
vii.https://journals.asm.org/doi/pdf/10.1128/JVI.00192-21
viii.https://pubmed.ncbi.nlm.nih.gov/32510973/
ix. https://journals.physiology.org/doi/full/10.1152/ajpcell.00426.2020
x. https://royalsociety.org/-/media/policy/projects/set-c/set-c-long-covid.pdf

2. New Tests for Mitochondrial Function



Mitochondria are tiny powerhouses sitting in each of our cells, producing our energy in the form of ATP – adenosine triphosphate. They make up around 40% of the volume of our heart; some neurons have ~ 2 million mitochondria each. One billion of them would fit in a grain of sand, yet, gram for gram, our mitochondria convert between 10,000 and 50,000 times more energy per second than the sun.

Our mitochondria have a myriad of functions: bioenergetics, biosynthesis, signalling. They are in many ways the true orchestrators of health and disease. Every disorder has a mitochondrial component, whether metabolic, neurological, cardiac or oncological. The mitochondria are responsible for switching between carbohydrate and fat metabolism, and can use ketones to supply the brain with energy alongside glucose. As a result of their key role, mitochondrial dysfunction is intricately connected with the emergence and therapy of many disorders.

The science of the mitochondria has been advancing at lightning speed in recent years, but it has been a challenge to find ways to measure the function and characteristics of these minute organelles. The Seahorse XF has opened up new diagnostic vistas: high-throughput respirometry has been developed that can dynamically assess the response of mitochondria to changes in their cellular environment. Multiple mitochondrial parameters are available that have the power to predict both disease progression and response to therapy. Since its introduction in 2006, Seahorse XF technology has been used in over 7,000 peer-reviewed publications.

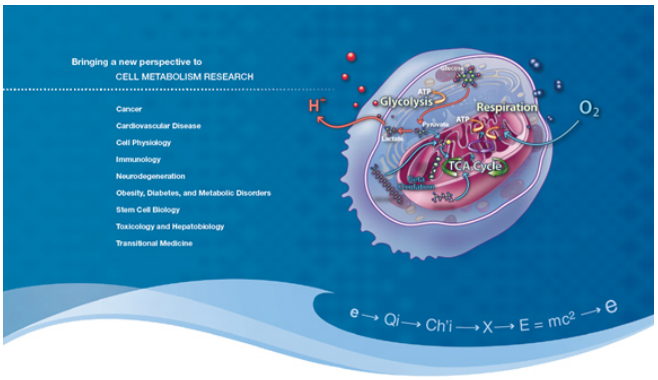


Figure 1
https://www.biochemmack.ru/upload/iblock/232/232bc36e1917c4b0ceaac6115cd2de6a.pdf

AONM is now able to offer a range of tests along multiple dimensions of mitochondrial and cellular performance using the Seahorse XF as well as extracellular flux analysis with luciferase assays.

The tests generally require only one vial of blood in a CPDA tube (supplied). The laboratory uses PBMCs (peripheral blood mononuclear cells, no centrifuging). AONM supplies the kit and organises the shipping.

AONM will be holding a series of mitochondrial webinars in the first quarter of 2022 where the tests will be described in greater detail. Please see our website for further details of these tests available https://aonm.org/mitochondrial-testing/.

Literature

Chacko, B. K. (2. May 2014). The Bioenergetic Health Index: a new concept in mitochondrial translational research. Clinical Science, S. 367-373.

Chacko, B. K. (24. Dec. 2015). The Bioenergetic Health Index is a sensitive measure of oxidative stress in human monocytes. Redox Biology, S. 43-50.

Chacko, B. K. (25. March 2013). Methods for defining distinct bioenergetic profiles in platelets, lymphocytes, monocytes, and neutrophils, and the oxidative burst from human blood. Laboratory Investigation, S. 690-700.Rousset, S. e. (Feb. 2004). The Biology of Mitochondrial Uncoupling Proteins. DIABETES, S. 130-135.

Nguyen, T. e. (15. May 2009). The Nrf2-Antioxidant Response Element Signaling Pathway and Its Activation by Oxidative Stress. Journal of biological chemistry, S. 13291-13295.

Austin, S. e. (2012). PGC1a and mitochondrial metabolism – emerging concepts and relevance in ageing and neurodegenerative disorders. Journal of Cell Science, S. 4963-4971.

St-Pierre, J. e. (20. Oct 2006). Suppression of Reactive Oxygen Species and Neurodegeneration by the PGC-1 Transcriptional Coactivators. Cell Press, S. 397-408.

Guo, W. e. (1. Jul. 2010). DNA Extraction Procedures Meaningfully Influence qPCR-Based mtDNA Copy Number Determination. Mitochondrion, S. 261-265.

Bordo, D. e. (3. Jun. 2002). The rhodanese/Cdc25 phosphatase superfamily. EMBO reports, S. 741-746.

Gliubich, F. e. (30. Aug. 1996). Active Site Structural Features for Chemically Modified Forms of Rhodanese. The Journal of biological chemistry, S. 21054–21061.

Hildebrandt, T. e. (29. Apr. 2008). Three enzymatic activities catalyze the oxidation of sulfide to thiosulfate in mammalian and invertebrate mitochondria. The FEBS journal, S. 3352-3361.

Spotlight on AONM's new ATP Profile

The ATP Profile measures total ATP production and allows a quantitative comparison of the cells' energy engines – mitochondria and glycolysis. The profile consists of the following markers:

a) Total ATP

The maximum quantity of ATP that the cells are able to produce at rest via both mitochondrial and non-mitochondrial pathways. Total ATP is all the adenosine triphosphate available to the cell. This makes it possible to assess the relative performance of anaerobic glycolysis versus mitochondrial respiration.

b) Mitochondrial ATP capacity

This is the rate of mitochondrial ATP synthesis in a defined basal state. Mitochondrial-generated ATP, if production is functioning smoothly, has a very high harvest: ~ 34 ATP from one molecule of glucose, and far more from fats (e.g., 146 ATP from one molecule of oleic acid). The result is given both as a percentage and in femtomoles/cell. A decrease within or below the specified reference range acts as a useful marker of mitochondrial function, and can be due to a number of factors such as lack of substrate availability, and/or damage to oxidative phosphorylation.

c) Glycolytic ATP capacity

ATP can also be produced in the cytosol, outside the mitochondria (though still inside the cell). This is produced largely from glucose, and the amount of ATP per molecule of glucose is very low (just 2 ATP per molecule of glucose). This parameter measures the glycolytic capacity for ATP production: the maximum quantity of ATP that the cells are able to produce at rest via non-mitochondrial pathways, i.e. anaerobic glycolysis. This makes it possible to assess the relative performance of anaerobic glycolysis versus mitochondrial respiration. The metric, again, is a percentage as well as femtomoles/cell.

d) Reserve ATP capacity

ATP synthesis is generally presumed to be coupled almost entirely to two metabolic processes: oxidative phosphorylation and glycolysis. There is however another essential metabolic process that interconverts the three adenine nucleotides (ATP, ADP and AMP) using adenylate kinase according to metabolic needs. Adenylate kinase catalyzes a reversible reaction: 2 ADP > ATP + AMP. This is a vital factor in regulating the energy charge in cells, and indicates how dynamically the cell is able to perform this catalytic interconversion.

Please see here for a sample of the results: https://aonm.org/wp-content/uploads/2021/08/ATP-Profile-Sample-Result-No.-1.pdf

3. Autoimmune Encephalopathy Secondary to Infectious Disease: A New Perspective on the Pathogenetic Interaction of the Immune System, Infection, Stress and Chronic Disease

February 9-11, 2022

An exciting virtual conference on autoimmune encephalopathy (also called PANS/PANDAS) is taking place on February 9-11. Guest speakers from around the world include specialists from Oxford, Columbia, Duke, and even the renowned Sheba Medical Center in Israel.

As the conference organisers write in their invitation to the event: "The ways in which we approach ME/CFS, neuropsychiatric disorders, PANS/PANDAS, chronic Lyme, fibromyalgia, and even long-haul COVID-19 need to change. What if these diseases aren't distinct? What if they are different manifestations of the same root cause – **immune dysregulation resulting in neuroinflammation?** And if they are, how do we successfully treat them?"

Early bird tickets if you do not wish to be awarded CPD points are available here hopehealingknowledge.com for $69 for all three days, until January 17th, after which the price rises to $99.

For medical professionals (with CPD included), the early bird until Jan. 17th is $325, and $375 afterwards: https://inevent.com/en/FoundationforTotalRecovery-1625240794/94-FoundationforTotalRecovery-1639074062/purchase.php

You can view the complete agenda and lineup of incredible speakers by clicking **here**.

AONM will be exhibitors at the event, we look forward to seeing you there!

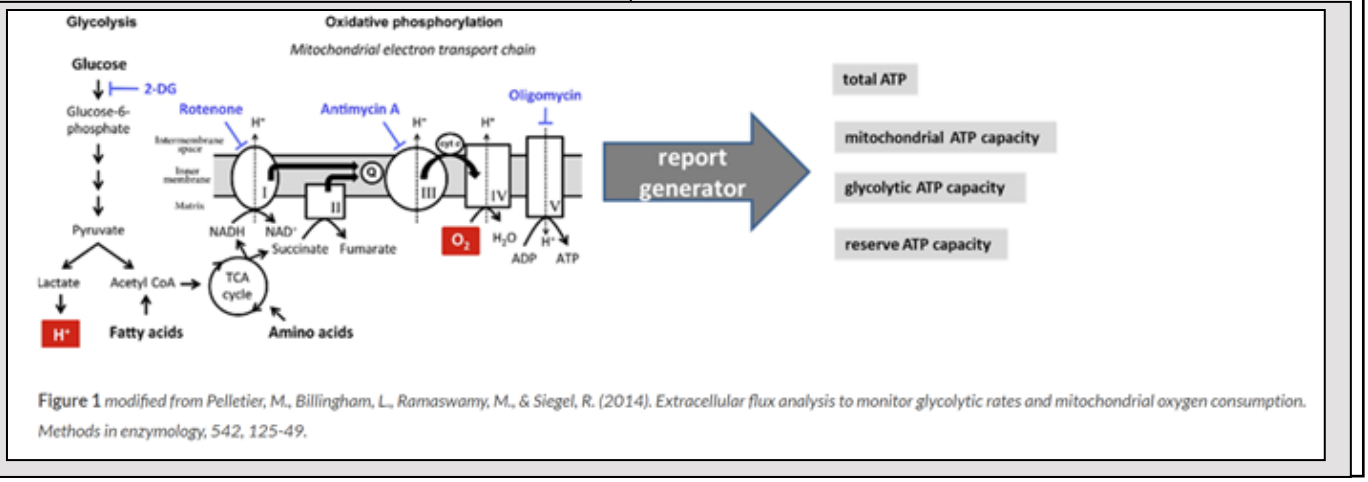
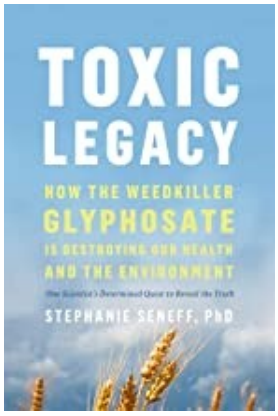


Figure 1 *modified from Pelletier, M., Billingham, L., Ramaswamy, M., & Siegel, R. (2014). Extracellular flux analysis to monitor glycolytic rates and mitochondrial oxygen consumption. Methods in enzymology, 542, 125-49.*

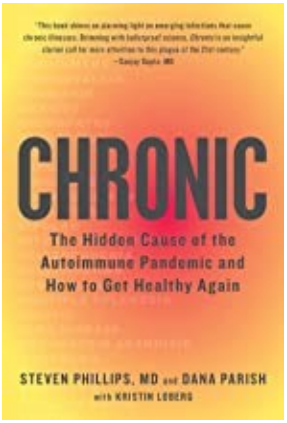
4. Book reviews

Toxic Legacy: How the weed killer glyphosate is destroying our health and the environment



This masterpiece is subtitled "One scientist's determined quest to reveal the truth". Professor Stephanie Seneff from MIT describes in this book the disruption of glyphosate – the most commonly used weedkiller in the world – on the gut microbiome, "its crippling effect on protein synthesis, and its impact on the body's ability to use and transport sulphur." Stephanie Seneff points out that though human cells do not possess the shikimate pathway, which glyphosate, the active ingredient in Roundup, disables, our gut microbes do. They use the pathway to synthesise tryptophan, tyrosine and phenylalanine. Imagine the impact that truncating this pathway is likely to have on numerous pathways that require these essential aromatic amino acids, from the thyroid, our substantia nigra to produce dopamine, through to our neurotransmitter serotonin and much more. Glyphosate's chelation properties also mean that it disrupts a plant's uptake of crucial minerals such as zinc, copper, manganese, magnesium, cobalt and iron. This leads to nutrient deficiencies in the food we eat. This is all quite apart from the pervasive potential harms of glyphosate: its mutagenicity, for example. A book very worth reading.

Chronic: The hidden cause of the autoimmune pandemic and how to get healthy again



In this stunning work "Chronic", Drs. Steven Phillips and Dana Parish provide stark evidence of prominent role that infections play in causing autoimmune disease, and offer multiple therapy options. They discuss a huge array of infections and the fallacies that can build up around them. They tear down the myth that autoimmune diseases are purely genetic, or have no known cause, instead summoning strong evidence that the key driver is often an infection. A large section focuses on "The big list of Lyme+": Borrelia burgdorferi and all its coinfections. "Today millions of people around the world are paying a heavy price for the failure of our medical community to recognise the pandemic in plain sight, and to address and treat Lyme+ properly."

Their chapter "Early treatment saves lives" on COVID-19 is also an inspiration. "First, prevention is key. Second, early treatment is associated with better outcomes. Third, advocate for yourself if you're not being heard by your doctor. And most importantly, never give up. … We are hopeful that COVID-19 will inspire the global community and clinicians to view chronic illness in a new and treatable light."

AONM TESTING SERVICES

For more detailed information please see our website www.aonm.org

Helping practitioners identify real causes of illness
Testing available for a range of chronic illnesses covering:

Lyme Disease and co-infections **Tests of Mitochondrial function**

Cancer monitoring: Testing for circulating cancer cells as well as likely apoptosis of cancer cells by natural and other substances to help practitioners determine effectiveness of ongoing treatment

PANS/PANDAS: Assisting practitioners to identify whether an individual's neurological and/or other symptoms could be caused by an autoimmune dysfunction

Food intolerances - various tests available

+44(0)3331 210 305 info@aonm.org

5. Upcoming events

AONM

Coming soon
Viral testing by Dr. Armin Schwarzbach
A series of webinars on mitochondrial testing with:
Dr. Brigitte Koenig
Dr. Sarah Myhill
Gilian Crowther

Klinghardt Institute

Autonomic Response Testing Level 1 online
18th January 2022
A.R.T. 1 Beginners Online Programme.

See www.klinghardtinstitute.com for further details and to register, plus other events.

BSEM

Training Day 11: Gastroenterology and Beyond
4th February 2022
Hallam Conference Centre
44 Hallam Street
London WIW 6JJ
https://www.bsem.org.uk/events/training-day-11-gastro-enterlogy

Annual Scientific Conference - Mould and Mycotoxins: Infections, Allergy and other Pathologies
The immunological and toxicological mechanisms will be examined, together with the practical issues of diagnosis and management. Friday 24th June 2022
https://www.bsem.org.uk/events/46-annual-scientific-conference-mould-and-mycotoxins-infections-allergy-and-other-pathologies

---

Autoimmune Encephalopathy Secondary to Infectious Disease: A New Perspective on the Pathogenetic Interaction of the Immune System, Infection, Stress and Chronic Disease

Early bird tickets if you do not wish to be awarded CPD points are available here
hopehealingknowledge.com
for $69 for all three days, until January 17th, after which the price rises to $99.
For medical professionals (with CPD included), the early bird until Jan. 17th is $325, and $375 afterwards: https://www.sw-online.com/vhalls/welcome-to-foundation-for-total-recovery/.
https://inevent.com/en/FoundationforTotalRecovery-1625240794/94-FoundationforTotalRecovery-1639074062/purchase.php

---

Biolab

Long COVID Day
25th March 2022
Holiday Inn Bloomsbury
Coram Street
London WC1N 1HT
Biolab announce that their next event, Long Covid Day, will be held on Friday 25 March 2022. This will feature practitioners presenting case histories as well as two Expert Panels to answer audience questions. This will be a hybrid event: both live at the Holiday Inn, Bloomsbury and on Zoom.
AONM's Gilian Crowther will be one of the speakers.
https://longcovidday.eventbrite.co.uk/

ANP

Covid-19 vaccinations: Round 3 Q&A
With Dr. Jayne Donegan, Dr Robert Verkerk & Dr. Elizabeth Evans
15th February, 6.30pm (online)
https://theanp.lpages.co/covid-19-vaccines-3/?utm_source=newsletter&utm_medium=email&utm_campaign=let_s_kick_off_2022_with_a_bang_anp_news&utm_term=2022-01-09

GNC

The GNC is running a series of naturopathic webinars. Its December webinar was a superb and very extensive presentation by Dr Jodie Dashore of BioNexus Health called "The BioNexus Approach to Autism Spectrum Disorders: Plant-based treatment options." This is available on the GNC Online Events page https://youtu.be/lS8B_bPI7bE