



इसुश्रुतऱ लडडलकल नडलड

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Wherever the art of medicine is loved,
there is also a love of humanity.
- Hippocrates

Sushruta Medical News

A Medical Newsletter of the

American Association of Physicians of Indian Origin

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Editorial

COVID-19 and Aerosols: The Impact on Healthcare Professionals

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The novel coronavirus, caused by Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), was reported in Wuhan, Hubei, China in December 2019. As of July 4, 2020, SARS-CoV-2 has infected over 11 million people and resulted in over half a million deaths globally (1). It has been reported that 275 physicians have died due to COVID-19 as of April 15, 2020 (2). Highest deaths were seen in general physicians and emergency room doctors. Pulmonologists, internal medicine specialists and anesthesiologists comprised 52% of those who died due to COVID-19. Dentists accounted for 6% of the deaths followed by ENT and ophthalmologists at 4% and 3% respectively.

The main mode of transmission is by respiratory droplets- contact via fomites or direct human contact. Aerosolized spread of the virus is still being researched and several studies referenced by the Centers for Disease Control show that SARS-CoV-2 is resilient in aerosol form (3, 4). An aerosol is defined as a suspension of fine solid particles or liquid droplets in air or another gas (5). Inside an aerosol, the nuclei of the viral droplet can remain in the air for longer periods of time and be transmitted to lengthier distances than a respiratory droplet, as long as the virus remains viable. These aerosols containing the virus are also called bioaerosols (6). These bioaerosols are not efficiently filtered by surgical masks, and more specialized equipment like the N95 mask, N99 mask and elastomeric respirators are used. It has been reported that viruses in aerosols are impacted by environmental stresses caused by humidity, temperature and sunlight before they reach a susceptible host (7) and these viruses can lose or gain viability and there can be a change in infectivity to some extent due to these environmental factors.

Airborne transmission may occur during aerosol-generating medical procedures (AGMP) (8). The possibility of airborne transmission occurring in the absence of AGMP is unclear. More in depth research is needed to ascertain the various modes of transmission of this disease with a focus on aerosols. However, the World Health Organization has suggested that some hospital procedures can generate aerosols that can be detrimental to healthcare professionals. A few of these procedures are endotracheal intubation, open suctioning, administration of nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, breach of the mucosa, thoracic surgery and cardiopulmonary resuscitation (9). To prevent the spread of this infection, the WHO has recommended a series of protocols to be followed in settings where COVID-19 patients are treated and quarantined (10).

Several physician specialty groups have published guidelines for treatment procedures specific to their specialty and recommended safety protocols as there is potential for transmission from symptomatic and asymptomatic patients (10-15). Difficulties in diagnosis and isolation of the patient for effective treatment are commonly seen. As the reliability of COVID-19 tests increase, assessment of COVID-19 status will most likely become standard of care before performing AGMP. Several types of PPE have been recommended by the WHO and CDC over the past few months for the protection of healthcare professionals when treating patients who are COVID-19 positive (10, 16). Since many patients are asymptomatic, similar procedures are recommended when performing AGMPs on asymptomatic patients as well.

The most commonly recommended respirators are the N95 disposable half mask filtering face-piece respirators (FFR) and in some cases N99 disposable masks. Elastomeric Particulate Respirators (EPR) are alternatives to FFR¹⁶. EPR are half face-piece or full face-piece tight-fitting respirators. The advantage of EPR is that it can be cleaned, disinfected, stored, and re-used. They are usually made of synthetic or natural rubber material. It is recommended that EPR be cleaned and disinfected immediately after removal. The CDC guidelines list 3 types of EPR: N-Series EPR are not oil-resistant; R-Series are somewhat oil-resistant, and, in industrial use, typically have an 8-hour use limitation and the P-Series are oil-resistant and rarely have use-time limitations (16). In the cases of trauma surgeons and health care professionals working with power tools, it is recommended that they use level 4 surgical gowns (level 4 gowns are used in high-risk procedures such as surgery or when infectious diseases are suspected), face shields or goggles, double gloves, N95-99 respirator masks. Operation facilities are also recommended to have HEPA filters in their ventilation system.

In many cases, several non-emergency procedures were deferred since the onset of COVID-19. As the lockdown eases, and more information is available regarding the virus and new innovation in disinfection procedures and containment of aerosols generated by AGMP are made available, the ultimate goal is to be able to perform routine AGMP without increasing the risk of contracting COVID-19 for both health care professionals and patients.

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Importance of Evidence-based Decision Making and Clinical Trials Participation in COVID-19 Era

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Everyone is talking about SARS-CoV-2 infection and related PPE donning and doffing, ventilators, ICU, new cases, deaths, loss of jobs, school and business closures, social distancing, restricted air travel and being locked at home, which was never heard of at this large scale affecting so many people so fast. Yes, it is real. So how are we to deal with it, to beat it, and get back to normal?

Here we propose that as medical professionals it is very important that we base our management decisions on evidence-based practice (EBP) and help in conducting clinical trials. Indian origin physicians are known in the USA to fill in the gaps in medical care needs of the nation. Both in primary care and academics, physicians of Indian Diaspora excel and are respected ([Torrey and Torrey, 2012](#)), and they contribute to the American Heritage. During these crisis-like situations with COVID-19 pandemic, AAPI members need to play very useful, yet thoughtful roles in terms of treatment, prevention and education related to COVID-19. It is not clear at this time which treatment works well. None of the current treatments are based on phase III, class I evidence. The syndromes and symptom-complexes associated with COVID-19 are just evolving. Given the above, AAPI and its leadership and members should support phase I, II and III studies vigorously. Here we present some crucial points on evidence-based medical practice and participation in clinical trials in COVID-19 era.

Based on SARS-CoV and MERS-CoV outbreaks, Carlyn Harris and associates have identified a list of evidence-based themes of clinical research areas that need to be prioritized in Covid-19 pandemic ([Harris et al, 2020](#)). These themes of research areas are listed in Table 1. An added theme should be – Clinical Trials Participation.

Table 1: Themes of Research Areas for Covid-19 Derived from SARS-CoV and MERS-CoV Experience

Source: [Harris et al, 2020](#)

1. Clinical Characterization
2. Prognosis
3. Clinical Management
4. Diagnosis
5. Viral Pathogenesis
6. Epidemiological Characterization
7. Infection Prevention and Control/Transmission
8. Susceptibility
9. Psychosocial

Sackett and associates defined evidence based medicine as, “*the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients*” in 1996 ([Sackett et al, 1996](#)). Many of the clinical trials in the past were flawed. Often importance was not given to clinical trial findings as much as biological reasoning and experience. In an editorial, Mark Ebell and associates point out many reasons why physicians do not practice evidence-based medicine promptly and consistently ([Ebell et al, 2018](#)). Those reasons are listed in Table 2 as well as some real-life examples of not following evidence in our daily practice as shown in Table 3.

Table 2: Reasons Behind Not Following Evidence in Daily Practice

1. **Practice Inertia:** I have been trained to practice this way and I have been practicing this way; why change now?
2. **Biological Reasoning / Pathophysiological Thinking:** It may appear logical to the mind to practice in certain way, although clinical trial evidences are against it.
3. **Economic Considerations / Lack of Industry Support:** When clinical trial findings are against the economic interests of the industry, the facts are not often publicized and get lost in the academic literature without reaching the attention of the practicing physicians. Recommendations by sub-specialty experts often can be biased.

Source: [Ebell et al, 2018](#)

Table 3: Examples of Some Practices That are Not Evidence-based

Modified from: [Ebell et al, 2018](#)

- Most patients are still told to fast before having their blood drawn, even though measurement of non-fasting lipids is a more accurate predictor of cardiovascular risk than fasting lipids
- Most physicians also still recommend routine home blood glucose monitoring even though numerous well-designed randomized trials have shown no benefit to daily measurement of blood glucose in patients with type 2 diabetes mellitus who are not using insulin
- Years after the release of guidelines to screen only average-risk women 21 to 65 years of age for cervical cancer every three to five years, many primary care physicians still recommend annual screening of older and younger women at average risk
- Although corticosteroids have been shown to safely reduce morbidity and mortality in hospitalized patients with community-acquired pneumonia, their use is not considered a standard of care in many U.S. hospitals

Call for Action: Here we call for action by AAPI and Indian Diaspora Physicians to rise to the occasion; participate vigorously in overcoming the COVID-19 crisis in the USA; help manage patients with COVID-19; develop guidelines based on evidence-based medicine; work with basic-scientists to develop translational measures to fight and improve outcomes from COVID-19; and most importantly help develop and participate in clinical trials. As there is so much to learn from our own physicians who are affected by COVID-19 and why it is affecting Indians, evidence-based medicine is the right path to tread.

Disclosure: Authors declare no competing interests.

References: Citations shown in the text are hyperlinks to the corresponding publications.

Call for Contributors

Potential contributors are welcome to submit their works for the following categories. Please enclose a portrait photo with your article along with your qualifications, city and state and email ID. **Email contributions to:** smn@aapiusa.org

- **A Piece of My Mind** (an opinion on current day medical and healthcare topics)
- **Bench-to-Bedside**
- **Bedside-to-Bench**
- **Review Articles on Important Subjects**
- **Clinical Dilemma**
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- **Pictorial Case Report**
- **Pictorial CME**
- **Medical Quiz**
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- **Veterans Health News**
- **Pioneers in Medicine and Healthcare**

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MSRF Longue

A General Surgery Intern in ICU during Peak of COVID-19

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As a PGY-1 in General Surgery during the peak of COVID-19, I worked a week in the ICU of Barnabas Medical Center, Livingston, New Jersey. Here are my experiences, impressions and thoughts, which I would like to share with you.

NEUROSURGERY: Sedate, sedate, sedate. We can't have these patients fighting with ventilators. Once intubated, these patients required relatively high levels of sedation. We typically opted for fentanyl and versed drips, but have used/ added propofol as well. We also used ketamine drips, and sub out fentanyl for dilaudid drips when necessary. Unfortunately, some of these decisions were driven by what's in stock – fentanyl, versed, and propofol were all in high demand worldwide. The bottom line – sedate the patient to the extent you can. If you're using a BIS monitor, we generally aim for a BIS of 30-60. On a related note, we've also pushed paralytics, and generally started a drip (preferably nimbox; but we used vecuronium as well) to paralyze all of the intubated patients we prone (more about proning below).

CARDIOVASCULAR: These patients immediately get a central TLC and an arterial line after intubation. All of their pressures drop at some point – either secondary to the disease process, positive ventilator pressure, and/or our own tendency to keep them dry – and at that point, we generally start a norepinephrine (levophed) drip. If we are lucky, all they need is a small amount of levo (up to 10 mcg/min) before weaning it off. If we were not lucky, other pressers we've added include vasopressin, phenylephrine, and angiotensin II. Please note, we've seen all sorts of arrhythmias develop in these patients. Keep an eye on those rhythm strips.

PULMONARY: Obviously the system most attended to, and why you should praise your respiratory therapists every day. These lungs aren't exactly like ARDS lungs – especially in patients with no comorbidities. These lungs tend to hold on to their compliance, at least in the beginning. There still is a lot of debate regarding ventilator settings, so I can only offer the setting I have seen – pressure control with PEEP at 15 & FiO₂ at 100%, aiming for tidal volumes of 450-550, adjust respiratory rate per the ABG and wean (FiO₂ before PEEP) as tolerated. Generally speaking, most healthcare providers are more comfortable with volume control and the ARDS protocol – low tidal volumes (4-6 cc/kg) and high PEEPs. I've seen that work too. I will add, however, that early proning does tend to improve oxygenation in these patients. It is unclear whether proning truly affects mortality in the long run. Our criteria for proning has been somewhat nebulous – in general, if FiO₂ requirements have not improved and it's within the first 3 days of intubation, we trial proning at least once. Important things to consider when flipping a patient: tubes, lines, and pressure points. We are lucky enough to have a dedicated flip team (consisting of mainly OR staff) that comes in the AM and the PM.

GASTROENTEROLOGY: These patients all get an OGT or NGT at the time intubation. We start feeds asap – ideally concentrated and continuous, or bolus feeds if the pump is unavailable. We start a bowel regimen on all our patients, since they usually are on high doses of opioids. We use PO Pepcid for stress ulcer prophylaxis when we can, but use PPIs as well. Luckily, not too many issues on this front – most of our patients tolerate enteral feeding just fine.

ENDOCRINOLOGY: All our patients have at least a Q6hr insulin lispro sliding scale on board. Some don't need it at all, while others come in with blood glucose in the 900s requiring an insulin drip. COVID seems to have a pronounced effect on glycemic control, possibly due to an inflammatory effect or response by the pancreas. Regardless, watch & treat those sugars – this is important for diabetics.

GENITOURINARY: For some reason, many of our patients develop acute renal failure that appears prerenal in nature. The dilemma lies within adequately hydrating the patient without fluid overloading them and potentially worsening any pulmonary edema/effusions – a fine line that presents differently for each patient. Some patients we bolus; some patients

we diurese; some patients we end up doing both. Insert a Foley's and closely monitor fluid balance. We essentially dialyze for only 3 problems (1) hyperkalemia (2) fluid overload or (3) severe acidosis. Despite our best efforts, so many of these patients require temporary hemodialysis (HD) vs. continuous renal replacement therapy (CRRT).

INFECTIOUS DISEASES: Obviously the data are limited here, and we are not quite sure yet what really works. Is this just a viral pneumonia? Or is it multiorgan failure secondary to some thrombotic and/or inflammatory cascade? The etiology doesn't matter as much in the critical care setting, but we obviously try our best to treat the underlying cause. Every patient got hydroxychloroquine (400 mg Q12h for the first two doses, then 400 mg daily after that) unless their QTs was well above 500 (I haven't seen anyone go into torsades yet). The rest of the care here has been variable. Some patients get azithro if we suspect an atypical infection; most patients get broad spectrum antibiotics if we suspected a superimposed infection. We've started clinical trials on IL-6 antagonists, and more recently have green-lighted convalescent plasma therapy. We will just have to wait and see what works.

HEMOTOLOGY: Almost all these patients come in with grossly elevated D-dimer and fibrinogen levels. If these patients need temporary dialysis, most of them have issues with clotting of dialysis filters and catheters. Even though the signs are pointing to an extremely hypercoagulable state, we still haven't seen much benefit to starting these patients on therapeutic anticoagulation. That being said, some of us suspect a large pulmonary embolus might be the final insult for our patients who suddenly desaturate, decompensate and die within minutes.

CONCLUSION: Treatment strategies are constantly evolving. People are dying, but we're also seeing people survive the acute phase of their infection, get extubated and subsequently walk out of the hospital. We absolutely cannot lose hope.

TAKE HOME MESSAGE: Do not lose hope and keep doing your best under all circumstances.

COVID-19 and the Eye

Click on the journal names to access the websites of the publications.

Research from India

COVID-19 Pandemic from an Ophthalmology Point of View

Parul Chawla Gupta , M Praveen Kumar , Jagat Ram

Postgraduate Institute of Medical Education & Research, Chandigarh, India

[Indian J Med Res 2020 May;151\(5\):411-418](#) doi:10.4103/ijmr.IJMR_1369_20

A Review of Long-Term Corneal Preservation Techniques: Relevance and Renewed Interests in the COVID-19 Era

Sunita Chaurasia, Sujata Das , Aravind Roy

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[Indian J Ophthalmol 2020 Jul;68\(7\):1357-1363](#) doi: 10.4103/ijo.IJO_1505_20

Potential Ocular and Systemic COVID-19 Prophylaxis Approaches for Healthcare Professionals

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[Indian J Ophthalmol 2020 Jul;68\(7\):1349-1356](#) doi: 10.4103/ijo.IJO_1589_20

Tele-ophthalmology: Need of the Hour

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[Indian J Ophthalmol 2020 Jul;68\(7\):1328-1338](#) doi: 10.4103/ijo.IJO_1784_20



Pioneers in Medicine and Healthcare

Willem Kolff, M.D., Ph.D.

(February 14, 1911 – February 11, 2009)

Father of Artificial Organs

Dr. Willem Johan Kolff, also known as Pim Kolff, was a Dutch physician, and a pioneer of hemodialysis as well as in the field of artificial organs. He made his major discoveries in the field of dialysis for kidney failure during the World War II, and in 1950 he immigrated to the United States, where he had a long and very illustrious and productive career.

As a Resident in Medicine at the Groningen University, Dr. Kolff had to treat a 22-year old man who was slowly dying due to chronic kidney failure. This prompted Dr. Kolff to start doing research on how to replace kidney function using an artificial organ. Using debris from downed war planes, an enamel bathtub, orange juice cans, used auto parts, and sausage casings, in 1943 Dr. Kolff built the first prototype dialyzer. Working with that and failing repeatedly, in 1945 Dr. Kolff successfully treated his first patient, a 67-year old woman suffering from kidney failure, using his home-made crude hemodialysis machine (see below). That ushered the Age of Artificial Organs, which saved the lives of millions of patients with acute and chronic kidney failure over the decades. During the WW II, Dr. Kolff built several hemodialysis machines, and after the war he donated them to hospitals in Europe. One of them reached Mount Sinai Hospital in New York City, which was used to perform the first human dialysis in the United States on January 6, 1948 under the supervision of Drs. Alfred P. Fishman and Irving Kroop. Today, with close to 500,000 ESRD (End-stage Renal Disease) patients on hemodialysis, each costing about \$90,000 per year to the Medicare System, hemodialysis is a major medical expenditure in the United States.

While in the United States, Dr. Kolff worked at the Cleveland Clinic, where he developed heart-lung machine. Later at the Brigham and Women's Hospital, Dr. Kolff produced prototypes of artificial kidney, which were manufactured commercially. In 1967, Dr. Kolff moved to the University of Utah as head of the Division of Artificial Organs and the Institute for Biomedical Engineering. There, he was involved in the development of the artificial heart, which was successfully implanted in 1982 in a patient Barney Clark. The patient survived for four months, with the heart still functioning at the time of her death. Later, Robert Jarvik, who worked with Dr. Kolff at the University of Utah developed the first permanent artificial heart. A brilliant physician and engineer, Dr. Kolff designed other artificial organs, including eyes, ears, and limbs, until his retirement in 1997. He was the founder of the American Society of Artificial Internal Organs. In 2003, Dr. Kolff was a co-nominee for Nobel Prize in Medicine and Physiology. Dr. Kolff left a rich legacy.

**Replica of the drum-kidney plus blood pump
first used successfully for acute dialysis
treatment in 1945 by Willem Kolff**



Picture: [Creative Commons Attribution-Share Alike 2.0 Generic](#)

Dr. Kolff and Dr. Scribner Share their ESRD Stories

<https://www.youtube.com/watch?v=WjQCd7Hi5YQ>



**For a Rich Collection of Dr. Kolff's Life and Contributions,
please visit his gallery at:**

<https://achievement.org/achiever/willem-j-kolff/#gallery>



The Discovery of Bower Manuscript: Right Place, Right Time

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Editors' Note: *Sushruta was a pride of India, especially for the medical professionals. Although well-known for his skilled surgical procedure for rhinoplasty, Sushruta was in fact a keen observing physician and pathophysiologist. Working about 2,500 years ago, he discovered diabetes mellitus (madhumeha) as a disease due to excessive sugar in the body. He also described obesity as a "disease" that leads to diabetes and heart diseases. He even prescribed dietary regimens and exercise to overcome these two ailments that are causing major health problems today. It should be noted that obesity has been officially recognized as a disease by the AMA in June 2013 only. In view of these historical facts this newsletter has been aptly named as Sushruta Medical News. What Hippocrates was to the Western Medicine, Sushruta was to the Indian Medicine, if not more. It is our duty to recognize our heritage in medicine. In this article, Dr. V. K. Raju presents how serendipitous discovery of Bower Manuscript opened up an entire treasure of ancient Indian Medicine and Surgery to the world. **Note:** Both Susruta and Sushruta are accepted spellings.*

The only thing new in the world is the history you do not know. – President Harry Truman

Today, both scholars and physicians study Ancient India and its teachings about medicine. We know, now, about the Golden Age of Surgery, which Susruta ushered in. For much of history, though, the Western world either didn't know or didn't care to know about Ancient India—at least not until the late 19th century, when one man made a discovery that would draw the attention of scholars across the globe and pique the world's curiosity about Ancient India. That man was Lieutenant Hamilton Bower, and his world-changing discovery was a complete coincidence. The Bower Manuscript, which was discovered by and named for Lieutenant Hamilton Bower, is "the oldest surviving manuscript on Ayurveda". Written on birch bark, it is believed to date back to the fifth century AD, but it was undiscovered in Kuchar until 1890. The manuscript mentions of eye drops, Susruta, and Charaka, a man sometimes called the Father of Medicine used. The manuscript is clearly a product of Ancient India. So how did it end up in Kuchar—and where is Kuchar anyway? And perhaps more importantly, how did Bower, an officer of the British India, originally sent to investigate a murder, come to find it?

Kuchar is in Central Asia; specifically, it's in Eastern Turkestan and was situated on "the great caravan route to China," which "skirt(ed) the foot of the Tien Shan Mountain Range." Long ago, Eastern Turkestan was a melting pot where the cultures of India, Western Asia and China met and mixed. In Kuchar, there was also a population of Buddhist monks, many of whom had made it their mission to carry Indian civilization and Indian literature into Central Asia. The Bower Manuscript was found in one of these Buddhist "viharas," or monasteries. Although some historians believe that the manuscript was written by monks in Kuchar, it was more likely written in Kashmir. Birch bark was commonly used as paper in North India, whereas palm leaves were used in South India. Although no one knows exactly how or why it ended up in Kuchar, we are lucky that it did, because the manuscript would have been much less likely to surface had it not been laid to rest in its dry, desert climate.

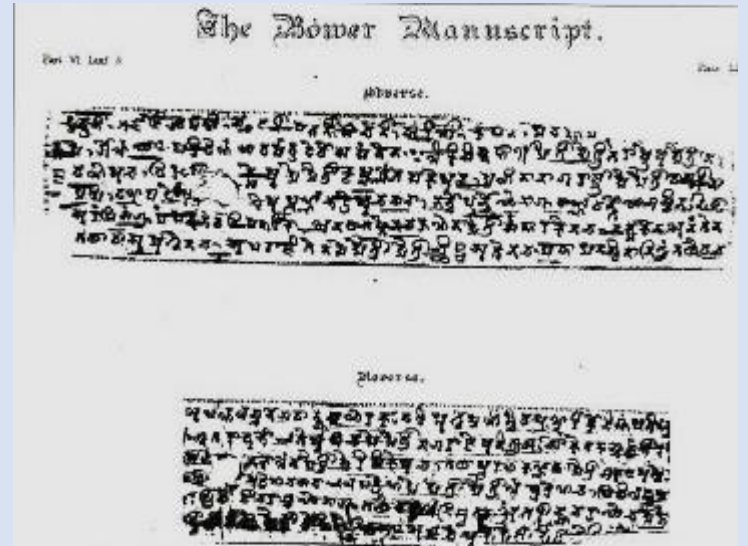
It was a sheer luck that the manuscript was found by a man who was able to recognize its importance and who shared it with great thinkers of the time. In fact, Bower was a textbook example of a man in the right place at the right time. He had traveled to Kuchar to find out who had murdered Andrew Dalgleish, a Scottish man who had set his sights on the mysterious Eastern world and had been shot for unknown reasons. Supposedly, while Bower was conducting his search, he was approached by a merchant of Kuchar. The Kuchari had teamed up with another merchant from Afghanistan, and together they had excavated a Buddhist monastery. There, they had found some treasures of the ancient world, including the manuscript that would soon be named for Bower. The merchants either gave or sold the manuscript to Bower, who sent it to the president of Asiatic Society of Bengal, a society established in 1784 to encourage "Oriental Studies." A.F. Rudolf

Hoernle, a member of the society, gave a brief outline of the contents of the manuscript in the society's April 1891 journal. According to Hoernle, the manuscript contains five distinct portions that appear to have been written by three different scribes. The first and longest portion of the manuscript contains "medical works." The second and fourth portions of the manuscript contain proverbs. The third portion of the manuscript contains a story about Buddha, and the fifth, which Hoernle claimed might be a fragment of a larger piece, concerns medical treatises.



Science Exploration Hall, Science and Technology Heritage of India Gallery, Science City, Ministry of Culture, Govt. of India.

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The discovery of the Bower Manuscript and the Asiatic Society of Bengal's presentation of it set off a long chain of events that would begin the modern movement of the archeological exploration of Eastern Turkestan, and encourage cultures around the world to begin their own searches for ancient manuscripts. For example, in 1891, The Russian Archeological Society contacted Nikolai Petrovsky, the Russian Consul General in Kashgar (a trading center also near the Tien Shan mountains) and requested that he begin a search for similar "treasures." What was then found and dubbed the "Petrovsky Collection" was exhibited at the Imperial Library in St. Petersburg. Similarly, a Moravian minister in Ladakh in the Kashmir region of the Indian subcontinent soon furnished the Asiatic Society of Bengal with manuscripts he had found in Central Asia. In 1893, the British government began making inquiries about ancient manuscripts in Kashmir, Ladakh, and Kashgar, and soon enough, the Japanese, Germans, Russians and French began exploring Kuchar too. Bower's discovery prompted worldwide interest not only in Central Asia, but also in Indian literature. In fact, some medical scholars believe that before the discovery of the Bower manuscript, "Indian thought had received but scant attention from medical historians," and some respected historians "still considered Hindus an inferior race." The Bower Manuscript also helped scholars learn more about Susruta and allowed them to claim with confidence that he lived well before the fifth century AD.

Thus, the discovery of the Bower Manuscript seems to have been the result of a string of happy coincidences. If the merchants who excavated the site of the Bower Manuscript hadn't given the artifact to Bower, would it still have found its way into the limelight? If Andrew Dalgleish had been murdered in Beijing instead of in Kuchar, would the manuscript have a different name-would we know about it at all? If the manuscript hadn't been brought to Kuchar, would it have perished long before anyone could find it? The discovery of the manuscript-indeed, the discovery of many things throughout history-now seems so accidental. But luckily for modern scholars and physicians, the manuscript was discovered, and that very accidental discovery ignited a global passion for the ancient world-and especially for India.

Historical Screw Up:

Some Western historians have questioned Susruta's influence-and whether he actually existed at all - perhaps because, as P. Johnson-Saint noted, "....our system of classical education had already given us an apparent beginning for all the arts and sciences. A disproportionate part of our education was devoted to Rome and Greece where we learnt all about Apollo [a revered Greek God who oversaw religious laws and morality] and Aesculapius [Apollo's son, the Greek God of medicine], and in Greek history, we came to Hippocrates. Here we had got a founder of medicine all ready for us, and that there might have been any one before, few of us were disposed to inquire."

Medical historian Dr. B. L. Gordon, writing in 1949, endorsed the claim that Indian medicine was already highly developed before the time of Alexander the Great. He critiqued the work of Dr. E. Haas, author of papers entitled "On the Origin of Hindu Medicine" and "Hippocrates and the Hindu Medicine of the Middle Ages." Haas, writing in 1876-1877, had conducted

a meticulous comparison of early Arabic texts with the few samples of medical text in Sanskrit available at the time. He dismissed claims that Susruta was an actual person, observing that his origins were clouded in mythology, and attributed the Susruta Samhita to the work of multiple scribes working between the tenth and fifteenth centuries AD. He remained a dedicated proponent of the primacy of Ancient Greek medicine and a dedicated skeptic of Ancient Hindu medical knowledge, asserting that all Hindu medical sciences were of Greek origin, preserved in Arabic by ancient scribes, and that the Susruta Samhita was merely a Sanskrit adaptation of Hippocrates. Dr. Haas is quoted as asserting that Susruta was in fact Hippocrates: "Nay, Susruta is himself none other than Hippocrates, whose name has been confounded with that of Socrates and misspelled Susruta." Haas continued in this vein by claiming that the birthplace of Susruta (Benares or Kasi) stands for Cos (the birthplace of Hippocrates), and that Susruta was ruled by his wife as Socrates was henpecked by Xanthippe. Dr. Haas's theory may well have been consistent with Europe's generally condescending attitude toward India and its people. But Dr. Gordon would have none of it. He notably wrote, "How one clever enough to read Hippocrates in the original and reproduce it in his own language could mistake the name of Socrates for Hippocrates surpasses one's imagination." Other Historians champion the Ancient Indians over Ancient Greeks. In fact, in Science and Secrets of Early Medicine, J. Thorwald asserts that nothing the Greeks produced in the field of surgery could remotely compare with the ideas of Susruta.

Disclosure: Author declares no competing interests.

For Further Reading:

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Scan QR Code for the Website

A One-Stop Website for COVID-19 Information

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As we are facing this exploding health care crisis of COVID-19 pandemic and inundated with a constant stream of information and misinformation, it is easy to be confounded and confused. It is not easy to navigate through this rapidly spiraling out landscape and timescale. So my approach to this escalating situation is to inform and educate myself as quickly as I can, while also going through daily clinical, family, social and other responsibilities and obligations. As I started collecting and reviewing as much open source information and data as available, it occurred to me that I should share this curated information with peers who are very busy and engaged in the frontline fighting this battle against COVID-19. So, I dedicated my website RAVIKOLLIMD.COM and redesigned it, posted numerous links to scientific and medical articles and public health resources. As I will be updating the site daily and frequently, I hope you find it of some value and use to you. Please stay safe and well.

Why is it Hard to Lose Weight as We Age?

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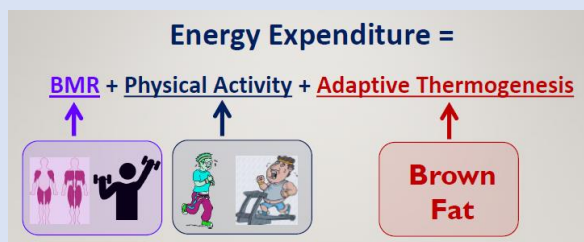
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One of the great challenges in the world is knowing enough about a subject to think you are right, but not enough about the subject to know you are wrong. – Neil deGrasse Tyson, Astrophysicist and Science Educator

Defining the Problem: Gaining belly fat is easy, but losing even a pound of it is very hard, especially when we are aging. It is a frustrating common experience for us, despite our knowledge of the science of overweight and obesity, and to some extent the aging process. What are the reasons? Recent developments in our understanding of nutrition, obesity, and energy homeostasis and the effect of aging on them strongly suggest that we are not understanding the problem in its correct sense and thus not doing the right thing. In our desperate attempts to find a universal solution as a tool to address the pandemic of obesity, we are oversimplifying the most complex issue of modern day life. The emerging concept that obesity is primarily a *disorder of broken energy homeostasis* ([Ghanemi et al, 2018](#)) is opening up an avenue to consider that food restriction or dieting or even physical exercise alone are not effective, but achieving an optimal energy homeostasis is needed for preventing the development of obesity. However, given today's environment with sedentary lifestyle in isothermic living conditions, and abundant food around, achieving the optimum energy homeostasis is easier said than done. Furthermore, cellular and molecular studies in animal models of diet-induced obesity are revealing several aspects of this condition, such as the potential irreversibility of certain cellular events beyond a certain point in the progression of obesity, loss of classical brown fat, decreased ability of browning of white fat and even whitening of brown fat, as we age. All these lead to a state of positive energy homeostasis, thus contributing to intractable obesity. In addition, age-associated decrease in muscle mass and BMR complicate the obese condition further, leading to the transformation of conserved energy into fat. This article presents state-of-the art information on the pathophysiology of obesity and thus provides a comprehensive knowledge of this condition from whole body energy homeostasis to cellular and molecular alterations that perturb the energy homeostasis. This article also provides insights into addressing the problem using the new knowledge gained, which may help us to deal with the problem of overweight and obesity in the clinics as it relates to aging process.

Energy Homeostasis: In an ideal state, energy (calorie) consumption vs. energy expenditure should be equal or slightly on the negative side. While most of us can compute the daily energy consumption to a reasonable degree of accuracy, it is hard to even guess the daily energy expenditure, especially as we are aging. Let us use the following equation and model to dissect the energy expenditure and then examine how aging process affects it.



BMR or Basal Metabolic Rate is the energy expended by the body at basal resting state. Muscle mass increases BMR.

Physical Activity expends ATP or calories.

Brown Fat burns the glucose and lipids and produces heat (thermogenesis), instead of ATP.

• **BMR or Basal Metabolic Rate** is the number of calories required to keep the body functioning at rest. It is similar to the gasoline consumed by a car while it is parked and the engine is idling. Just like the consumption of gasoline by an idling car depends on the size of its engine (V4, V6, V8, etc.), so also BMR depends on the size of our body, or more precisely the muscle mass, where most energy is utilized at rest. As we age, we gradually lose our muscle mass, and so the BMR keeps falling. When that is happening, even if we do not increase calorie consumption, we will be still in positive energy balance. For example, a male adult with a height of 5' 6" and weight of 160 lbs will have a computed BMR of 1,628 calories/day at age 30 years and 1,528 calories/day at age 50. That is a difference of 100 calories/day. Assuming that the person is eating the same amount of calories and has the same degree of physical activity at both age 30 and 50 years, he will gain 10.4 lbs in a year (3,500 calories = 1 lb fat), just due to age-related fall in the BMR. If that person is eating 100 calories/day more or

utilizing 100 calories/day less in physical activity at age 50 years, then he will put 20.8 lbs weight in a year. We often ignore this simple fact. To preserve the age-associated skeletal muscle mass, one has to do resistance or tension exercises or lift weights. These exercises that increase muscle strength and mass also significantly improve insulin sensitivity ([Shaibi et al, 2006](#)). It should be noted that skeletal muscle insulin resistance is considered to be the initiating or primary defect that is evident decades before β -cell failure and overt hyperglycemia develops leading to type-2 diabetes mellitus ([DeFronzo and Tripathy, 2009](#)). In this context, both men and women are equally benefitted by resistance exercises.

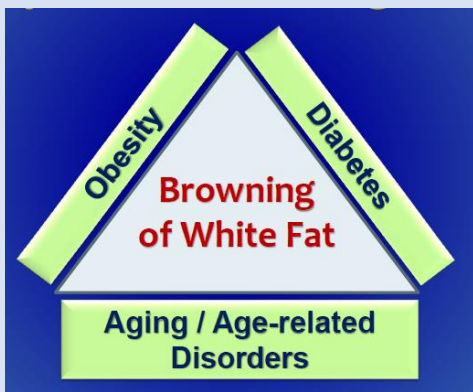
Although physical aging does not show up until late in the life, cellular senescence starts as early as at 40 years of age, and progresses slowly if there are no comorbid conditions ([Childs et al, 2015](#)). It is not only the loss of muscle mass, but also age-associated decrease in mitochondrial number due to reduced mitochondrial biogenesis that accounts for the fall in BMR with the progression of age. Just like the horsepower of a car engine decreases with increasing mileage due to wear and tear of cylinders, pistons and valves, so also the age associated decrease in mitochondrial number and biogenesis causes decreased energy utilization, leading to positive energy balance. Accurate calculation of BMR for individual subjects is not that simple as shown in the generic BMR calculators that take into account only age, gender, weight and height of the subject. To account for individual variations, the Harris-Benedict equation was introduced, which multiplies the computed BMR by a factor that corresponds to the level of physical activity of the individual ([Frankenfield et al, 1998](#)). However, one has to take into account weight history and ethnicity also to arrive at more accurate number for BMR ([Douglas et al, 2007](#)). The accurate calculation of BMR may assist in achieving weight loss by adjusting the calorie intake accordingly.

• **Physical Activity:** This is more straightforward to understand, monitor and quantify. It is also under our control. Physical activity can be in any form, such as brisk walking, jogging, swimming, skiing or cardiovascular workout. While these types of activities also improve the muscle mass, they cannot match tension exercises or weight lifting in increasing the strength of the muscle mass and improving insulin sensitivity. However, they do prevent loss of bone density by improving blood circulation in and around bones. Furthermore, jogging or swimming or such types of endurance activities improve the capacity of cardiovascular system and burn glucose and metabolites, and thus help to improve glucose homeostasis. The most practical use of physical activity or exercise is to ensure optimal energy balance by burning excess calories and improving the physical strength. Excess calories are converted into the ATP. When excess ATP is not used for activity, it induces the pluripotent mesenchymal stem cells (MSC) to differentiate into pre-adipocytes, which will give rise to adipocytes through a process of adipogenesis. But the same MSC can also differentiate into myocytes and osteocytes if a person is doing regular exercise, and thus build muscles and bones instead of belly fat. Excess ATP is just like excess money in our hands beyond our routine needs. It can be invested property or spent on a shopping spree or simply used in gambling. Each of these three have their own consequences on our long-term finances. So also, by using excess ATP wisely, we can invest in our long-term health and longevity. In observational studies, higher levels of physical activity or exercise are related to longer telomere lengths in various populations, and athletes tend to have longer telomere lengths than non-athletes ([Arsenis et al, 2017](#)). However, when a person reaches age 50 years, vascular senescence sets in with negative impact on cerebral, cardiac, and neuromuscular structure and function, which detrimentally affects physical performance ([Mendonca et al, 2017](#)). This is the phase of life when everyone has to choose a physical activity or endurance exercise that suits his/her body well without feeling stressful, to counter the age-associated vascular senescence and do it on regular basis. Vascular aging can be countered by regular physical exercise ([Ross et al, 2016](#)). Recently, it has been found that a small peptide called **irisin**, released from the skeletal muscles during exercise has a profound effect on whole body energy homeostasis and insulin sensitivity and glucose metabolism ([Arhire et al, 2019](#)). Hence, regular physical activity has benefits beyond the number of calories burned. This also emphasizes the fact that just consuming less calories is not sufficient to maintain good health, but one has to exercise on regular basis and thus actively use the whole musculoskeletal system. That is how our biology works.

• **Adaptive Thermogenesis:** It is regulated production of heat in response to external conditions, such as temperature or some foods, resulting in metabolic inefficiency. Because, heat is produced by burning metabolites, which could have otherwise generated ATP. It is similar to a car engine losing its efficiency and burning gasoline without giving enough mileage or even low mileage than expected. In recent years, adaptive thermogenesis has become a hot area of both basic science research on energy homeostasis and in anti-obesity drug development industry. There is nothing superior if we can simply burn away excess calories consumed through adaptive thermogenesis, rather than trapping them in the form of ATP, which will eventually become fat. In this context, adaptive thermogenesis is like an incinerator that burns all unwanted materials, without utilizing the heat thus produced for useful work. Adaptive thermogenesis is seen in all warm-blooded animals. There are two types of adaptive thermogenesis. One is shivering type, which is produced by rapid contractions of muscles in adults when exposed to cold weather. The other is non-shivering thermogenesis, seen in lower vertebrates, such as rodents, which are exposed to elements. The non-shivering thermogenesis is due to brown fat.

- **Brown Fat:** Central to the non-shivering thermogenesis is the brown fat. Brown fat is a specialized fat tissue, low in triglycerides and rich in mitochondria, which imparts a brownish tinge to it. Brown fat burns glucose and other metabolites, such as blood lipids, and produces heat, instead of ATP. Thus, brown fat creates negative energy balance, and promotes leanness. It is achieved by the presence of uncoupling protein-1 (UCP-1), which is unique to the brown fat and cannot be found in any other cell in the body. UCP-1 uncouples oxidative phosphorylation from the electron transport chain in the mitochondria. In human infants, non-shivering thermogenesis is due to brown fat depots. Infants' muscles are not fully developed to produce heat by shivering. As we age, the brown fat depots gradually decrease, resulting in the loss of adaptive thermogenesis capability. However, the rate of decrease of brown fat varies from one person to person, and can be influenced by comorbid conditions. In addition, environmental pollutants ([Di Gregorio et al, 2018](#)) and chronic alcohol consumption ([Blainer et al, 2017](#)) decrease brown fat content in adults. These are some of the reasons why we keep on gaining weight easily as we age, despite we do not increase the calorie consumption. The incinerator is not working efficiently to burn unwanted calories or metabolites as we age. Recently, it has been shown in rodent models that exposure to cigarette smoke during neonatal period induces lower brown fat thermogenic capacity, which can be obesogenic at adulthood ([Peixoto et al, 2018](#)). This finding has significant impact of maternal smoking on the human infants. Brown fat depots in the body can be visualized by PET scans. There are excellent review articles published on adaptive thermogenesis for further reading ([Müller and Westphal, 2013](#); [Reynés et al, 2019](#); [Major et al, 2007](#); [Celi et al, 2015](#); [Chouchani et al, 2019](#)).

- **Browning of White Fat:** Brown and white fat cells are derived from different progenitor cells. Attempts to induce expansion of canonical brown fat cells in adults were not successful. However, several years ago, scientists discovered that under certain circumstances white fat cells can be induced to change to brown fat cells, the so called "browning of fat". The resulting brown fat cells are called beige or brite (brown in white) cells. This observation has given a hope and ushered a new era in obesity research and drug development. Scientists across the globe described that browning of white fat is the "Holy Grail of energy metabolism" or "metabolic renaissance" or "quantum leap in aging research". Recent studies have revealed that browning of white fat not only helps to lose weight or prevent obesity, but also restores glucose homeostasis and may even slow down the aging process. ***This essentially makes browning of white fat as the unifying factor for the prevention of obesity and diabetes as well as slowing down the aging process and lessening the age-associated maladies as shown below.***



Emerging central role of brown fat or browning of white fat in combating obesity, diabetes and aging process and reducing the severity of age-related disorders.

Obesity: We have already seen how brown fat counters the development of obesity.

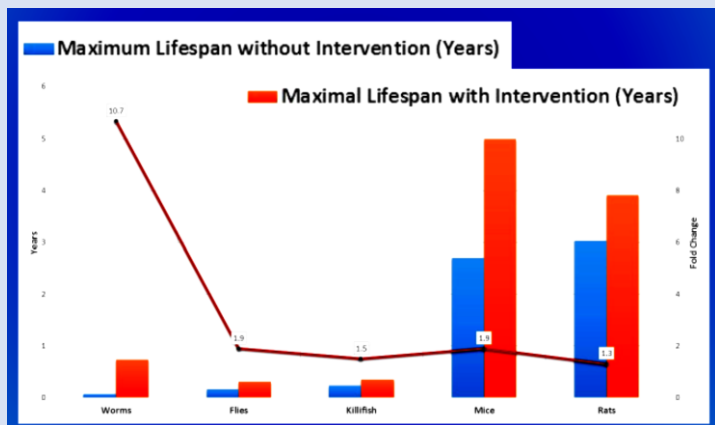
Diabetes: Brown fat regulates glucose homeostasis and insulin sensitivity ([Stanford et al 2013](#)). Browning of white adipose tissue uncouples glucose uptake from insulin signaling ([Mössenböck et al, 2014](#)). In non-obese mouse models, type-1 diabetes mellitus was reversed in an insulin-independent manner by allogenic brown adipose tissue transplantation ([Gunawardana & Piston, 2015](#)).

Aging: In animal models, aging process is associated with modeling of brown adipose tissue, and loss of browning of white fat ([Goncalve et al, 2017](#)). Evidence is emerging that increased brown adipose tissue activity may combat aging process and confer longevity ([Darcy & Tseng, 2019](#)).

- **Whitening of Brown Fat:** This phenomenon by which brown fat cells lose mitochondria and UCP-1 and become whiter due to accumulation of lipids, has profound implications on obesity, glucose homeostasis, and aging process. Being a high energy tissue brown fat is highly vascular. Vascular rarefaction, such as the one that occurs with aging process, has been shown to be a significant casual factor in whitening of brown fat. Vascular insufficiency in turn leads to mitochondrial dysfunction and loss of brown fat, resulting in systemic insulin resistance ([Shimizu and Walsh, 2015](#); [Lapa et al, 2017](#)). While whitening of brown fat leads to obesity, high fat diets can also cause whitening of brown fat. In rodent models it has been shown that the UCP-1 levels in the brown fat depend on the fat content of the food and duration of feeding high-fat diet. Thus, it seems that while modestly fatty foods and shorter duration of feeding may increase UCP-1, higher fat content of the food and/or longer duration of feeding are likely decrease the UCP-1 protein content of brown fat ([Fromme & Klingenspor, 2011](#); [Ohtomo et al, 2017](#)). This phenomenon may explain why morbid obesity in humans is very hard to treat or manage.

● **Role of Microbiota:** It is increasingly recognized that the gut microbiota influence our overall health and energy homeostasis and plays critical roles in disease conditions, including some mental disorders ([Davis, 2016](#); [Clapp et al, 2017](#)). A study published in 2016 in Obesity Research and Clinical Practice determined whether the relationship between calorie intake, macronutrient intake, and physical activity with obesity has changed over time to account for rise in obesity in the United States. The study examined data from 36,377 US adults from the National Health and Nutrition Survey between 1971 and 2008. The study concluded that factors other than diet and physical activity may be contributing to increase in BMI over the time ([Brown et al, 2016](#)). Although several factors, such as increased use of prescription and OTC medications, increase in the amounts of pesticides and environmental toxins can be contributing factors, some experts believe that a change in the gut microbiota of Americans occurred in 1980s due to rapid rise in consumption of fast foods and processed foods, thus triggering an obesity epidemic which is snowballing over the time. While more experimental data is needed, these observations underscore the importance of consuming probiotic foods and maintaining healthy gut flora in any anti-obesity program.

Is Aging a Natural Process or Disease? The above studies and experimental data from animal models are raising questions whether aging is an inevitable natural process or a disease. [Biogerontology Research Foundation](#) not only argues that aging is a disease, but also presents intriguing data from animal models to support its stand. A new generation of researchers called Biondemographers come with the belief that aging is a disease, and it should be officially recognized as such with its individual code in the International Statistical Classification of Diseases and Related Health Problems (ICD) ([Gavrilova & Gavrilova 2017](#); [Bulterijs et al, 2015](#)). In humans, aging and age-related disorders are intricately related. Aging process makes humans susceptible to diseases and conversely, diseases also accelerate normal aging process.



From [Bulterijs et al, 2015](#), [Creative Commons Attribution 4.0 International](#)

In this respect, animal models offer better perspectives, as most animals do not have comorbid conditions that drive aging process forward. As shown in the left, in five different species of animals, namely (Lt to Rt) worms, flies, killifish, mice and rats, interventions to slowdown the aging process clearly prolonged the lifespan., thus supporting the argument that aging is a disease. If aging is not a disease, but a natural biological process, the interventions should not prolong the lifespan. Biondemographers believe that recognition of aging as a disease will stimulate research by funding and thus result in the development of new efficient drugs to counter aging process.

Can Browning of Fat Help Us to Achieve Healthy Aging, Free from Obesity and Diseases like Diabetes?

It seems we are not far away from achieving that goal, thanks to rapid advancements in our understanding of energy homeostasis and discoveries and interventions that augment browning of white fat. Browning of white fat is the heat sink which can streamline our energy balance as we age. Meanwhile, let us examine the drugs and foods that can enhance browning of fat and expand the heat sink.

Factors that Induce Browning of White Fat: (Not Suitable as Therapeutic Agents)	Foods that Induce Browning of White Fat (Can be Used with Discretion)
<ul style="list-style-type: none"> Controlled exposure to cold (66° F) β₃-adrenergic stimulation Nuclear receptor (PPARγ) agonists (glitazones) Catecholamines Thyroid hormone Sex Steroids 	<ul style="list-style-type: none"> Short-chain fatty acids (modest amount of ghee or high-fiber diet) Ketogenic diet (not advisable for long-term use) Capsaicin in chili pepper Curcumin in turmeric Green tea extracts (including decaffeinated ones) Resveratrol in red wine (including alcohol free ones)

Disclosure: The author is a Co-Founder, President, CEO and Chief Scientific Officer of [ePurines, LLC](#), a startup company specializing in the development of purinergic based drugs for the treatment of obesity, and kidney and liver diseases.

References: Citations shown in parenthesis in the text are hyperlinks to the corresponding publications.