Editorial

November is Lung Cancer Awareness Month

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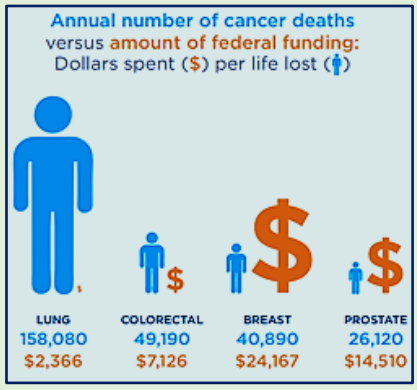

Source: Lungevity.org

Did you know that November is Lung Cancer Awareness Month? Most people are occupied with Elections, Autumn Leaves, Football, Thanksgiving, Black Friday, and of course, Diwali! Despite lung cancer being the most common cause of cancer deaths in the US and the world, amongst men and women; lung cancer awareness remains in the dark. Lung cancer is responsible for about a third of cancer deaths, yet it barely receives 10% of cancer research funding in the US. Prior to the pandemic, the American Cancer Society predicted almost 230,000 new patients of lung cancer and 135,720 deaths (more than from breast, prostate and colon cancer combined). The current pandemic has been a further setback for lung cancer.

Due to COVID-19, there has been a significant disruption in cancer care and diagnosis, including an alarming decline in lung cancer diagnoses. The rate of diagnosis had been relatively stable 13 months before the pandemic, but even at the end of April, when most quarantine restrictions were lifted across the nation, there was a 46.8% decrease in new lung cancer diagnoses (London et al, 2020). This was even worse in states hard hit by COVID-19. Nationwide, the weekly number fell 46.4% (from 4310 to 2310) for the top 6 cancers combined, including lung cancer (Kaufman et al, 2020).

Unfortunately, this decline is not due to decreased incidence but rather a delay in diagnosis. In some cases, people may still remain undiagnosed. These delays mean that future lung cancer patients are even more likely to be advanced at the time of diagnosis, which adversely impacts survival and prognosis. In the UK, a 5% increase in deaths at 5 years due to COVID-19 related diagnostic/treatment delays is expected (Maringe et al, 2020). Here in the US, an estimated a 6–7.7% increase in the number of deaths are predicted in the first year and over 20k years of life lost (YLL) are estimated from additional deaths due to cancer at 5 years. The good news is we can do something about it!

Early detection is key. Early stage lung cancer is usually asymptomatic, which is why screening is such an important tool. The low dose CT scan is designed to dramatically reduce patient's radiation exposure compared to diagnostic CTs, while still being highly sensitive for early stage lung cancer. It is a non-contrasted study which takes less than a minute. No labs are required, however an order from a healthcare provider is required. It is now covered by most insurances, including Medicaid in most states. As physicians we need to be more proactive about encouraging at risk patients to get scanned. It's much more convenient and pleasant compared to a mammogram, colonoscopy, or rectal exam, yet screening rates for lung cancer are far behind. Over 70% of eligible women have had a recent mammogram compared to less than 6% of patients eligible for a screening lung CT (Lung Cancer Screening – CDC 2020). Eligible patients are asymptomatic, aged 55 to 80 who have a 30 pack a year smoking history, including those who quit within the past 15 years.

Lung cancer treatment has also progressed which again is impacting patient outcomes positively. Robotic surgery allows more patients to get curative resections with much faster recovery times, which also reduces delays in adjuvant treatment initiation. Stereotactic body radiation therapy (SBRT) allows patients that are not surgical candidates to get treatment. The most publicized advance has been with chemotherapy. Immunotherapy and targeted chemotherapy options are increasing the life expectancy of patients with advanced disease. Patients who previously were given months to live are now living for years with reasonable quality of life. All these advances have led to a gradually improving trend in lung cancer survival.

One of the biggest obstacles is the stigma. It is not a "PC" cancer. Our first reaction when hearing someone is diagnosed is to wonder about their smoking status. While smoking remains by far the most common cause of lung cancer, the patient is still a person who deserves empathy and not blame. Ultimately, *NOBODY DESERVES CANCER.* We have to work as a medical community to shine light on lung cancer as we did with breast cancer. We must use our voice to improve awareness, screening rates, and research funding. Let's start talking about lung cancer!

References: Citations shown in the text are hyperlinks to their respective publications.
Disclosure: Author declared no competing interests.

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- **September 2020** https://www.aapiusa.org/wp-content/uploads/2020/09/SNM_September-2020_081020.pdf
- **October 2020** https://www.aapiusa.org/wp-content/uploads/2020/10/SMN_Octoberr-2020_Final.pdf

Dr. Sandeep Chilakala

Helping Babies Breathe (HBB)

Giving Newborns a Chance at Life

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Neonatal Mortality – Global Burden and Trends: Poor perinatal outcomes are a significant global health burden. Each year, approximately 2.7 million newborns die during the neonatal period (first 28 days of life) and another 2.6 million are stillborn. Many of the stillbirths are non-resuscitated neonates that subsequently die. More than 90% of these deaths occur in developing countries largely from preventable causes (Gaffey et al, 2015). Additionally, 300,000 women die annually around the world during pregnancy and childbirth.

From 1990 to 2015, global neonatal mortality rate (NMR) declined 47%, from 36 to 19 per 1000 live births. Between 1992 and 2016, the NMR in India declined from 49 to 30 death per 1000 live births (Singh et al, 2019). Current NMR for India is 21.6 and for the USA 3.8 per 1000 live births. The United Nations Sustainable Development Goals include a reduction in NMR to <12 per 1000 live births for all countries by 2030 and Every Newborn Action Plan extends this ambitious improvement to a global NMR of <10 per 1000 live births by 2035 (Collaborators, 2016).

The three most common causes of neonatal deaths worldwide are complications of preterm birth (35%), intrapartum-related causes including asphyxia (24%), and sepsis (15%). The first 24 hours account for more than one-third of the deaths that occur in the entire neonatal period. Asphyxia related neonatal deaths are a major concern and almost all deaths due to asphyxia occur in the first week of life with 70% of them occurring in the first 24 hours (Baqui et al, 2006). This has led to an intense global focus on interventions to help newborns who are unable to spontaneously initiate breathing at birth.

Globally each year, approximately 10 million newborns do not breathe spontaneously immediately after birth and would die within minutes without help. The first minute of life also called "golden minute" is extremely important to provide basic resuscitative measures to help the newborn breathe and prevent neonatal mortality (Goudar et al, 2013). Around 85% of term newborns breathe spontaneously within 10 to 30 seconds of birth, an additional 10% require initial steps such as tactile stimulation or airway clearing or positioning and approximately 3% require positive-pressure ventilation by bag and mask (Perlman & Risser, 1995). Any adverse events that happen in the first minutes after birth may have long term consequences on growth and development.

Most of the births in resource limited settings are facilitated by a birth attendant who is responsible for both the mother and baby. These birth attendants generally lack formal training and education in necessary basic newborn resuscitation skills that are critical for newborn survival (Steele, 2013). Many neonatal deaths in developing countries could be avoided with simple, low-cost interventions that address the needs of women and newborns at birth. Training the birth attendants in basic resuscitation measures including appropriate stimulation, clearing of the airway, and avoidance of hypothermia will help 90% of the newborns who are unable

to take a spontaneous breath at birth. These measures are extremely useful in limited resource countries with minimum or no access to healthcare during the delivery of an infant.

Neonatal Resuscitation – How Times have Changed: At first standardized training program for resuscitation of newborns at birth, the Neonatal Resuscitation Program (NRP) was released in 1987 jointly by the American Heart Association (AHA) and American Academy of Pediatrics (AAP) with a goal to have one professionally trained person in NRP be present at delivery. Many countries implemented the simplified NRP as they saw fit according to their available resources and several initiatives were taken to reduce neonatal and perinatal mortality.

In 2006, AAP organized a global implementation task force, which included stakeholders from a variety of disciplines committed to worldwide reduction in neonatal mortality and introduced a standardized algorithm, the Neonatal Resuscitation Program (NRP). The NRP algorithm can be complex to teach and implement in low resource settings. The International Pediatric Association congress in Athens in 2007 proved pivotal in establishing a radically different educational approach to teach resuscitation of newborn in low resource settings and developing nations. A simplified curriculum, but still with a goal of having a skilled person at every birth was developed. The result of this is **HELPING BABIES BREATHE (HBB)** that became available in 2010.

HBB is a simplified, evidence based pictorial resuscitation algorithm for use in low- resource settings which contains low cost simulation models and resuscitation equipment to disseminate both training and provision of care, (Helping Babies Breathe) The algorithm contains essential basic steps of infant resuscitation during the golden minute after birth to establish breathing. This includes drying, clearing the airway and Bag Mask Ventilation (BMV) with room air and the order in which they are to be performed. More advanced interventions such as chest compressions, intubation etc. were omitted. The different colors in the algorithm indicate the level of the intervention the baby needs after birth. Different levels of education and literacy of the birth attendants were taken into consideration during its development. HBB has empowered midwives and front-line birth attendants to provide a quality neonatal care at birth. This was an elegant solution to address intrapartum asphyxia, a common cause of preventable newborn mortality in developing nations. It also highlighted the importance of normal neonatal transition with interventions to maintain warmth via skin-to-skin contact, delayed umbilical cord clamping and initiation of breast feeding soon after birth.

Trained birth attendants participate in a training workshop. Along with the education and training in basic resuscitation skills, HBB also provides equipment necessary for bag-mask-ventilation and low-cost high-fidelity simulators. The attendants will become the providers of HBB with knowledge and skills to help babies to breathe on their own, giving them the gift of life.

To address the additional causes of mortality in neonates, other programs like Essential Care for Every Baby (ECEB), Essential Care for Small babies (ECSB) were developed by AAP using the same educational principles as HBB. ECEB was started in 2014. The curriculum begins after birth throughout the first day of the newborn's life, until the time of discharge. ECSB was started in 2015. This teaches the special care needed for small or premature babies born in low resource areas – so birth attendants and mothers learn how to keep babies warm by skin-to-skin wrapping and keep them nourished via alternative feeding methods.

The three programs, HBB, ECEB, ECSB together are called **Helping Babies Survive (HBS)** which has interventions to prevent the most common causes of preventable neonatal deaths, asphyxia, infection, and prematurity. Since its inception, >850 000 birth attendants in 80 countries have been trained and the curriculum has been translated to >27 languages. HBB is updated on a 5-year cycle beginning with second edition, which was released in 2016 and currently celebrating a decade of its implementation.

Future interventions and strategies should emphasize not only on newborn survival but on high quality survival. In-situ education programs should be implemented in the future. With the Coronavirus pandemic and

uncertainty about its duration, there are many innovations in healthcare education, training, and technology. Keeping up with the pace of technology, newer methodologies of education like video resources, self-paced learning, use of electronic platforms etc. are being used to promote current science and augment educational effectiveness. Novel newborn resuscitation trainers as well as mobile health solutions like tablets and digital applications are being used and newer technologies are being developed to help improve the simulation-based learning and eventually improve the skill retention (Prakash et al, 2016: Schaeffer et al, 2016). There should be ongoing evaluation of the effectiveness of these programs and integrate quality improvement measures both at regional and national levels. This will enhance the effectiveness of these programs and ultimately reduce the neonatal mortality and morbidity.

Summary and Conclusion: HBB in the past decade had an immense impact in saving lives of newborns across the globe. The intervention resulted in significant decrease in fresh stillbirths, all-cause mortality within 24 hours of birth and cause-specific mortality due to intrapartum-related events through discharge or 28 days (Niermeyer, 2017). Late neonatal mortality remained unchanged. These data show that in addition to the basic resuscitation at birth, ongoing neonatal care including respiratory support with supplemental oxygen, thermal support with kangaroo mother care, nasogastric feeding of breast milk and aggressive infection prevention/treatment strategies for more vulnerable infants are core functions that can improve survival without full neonatal intensive care. These steps will help sustain the gains in survival after basic resuscitation.

The desired ultimate goal is that every newborn no matter where in the world he or she is born, will be attended to by a person who will carry out effective resuscitation. That will be a reality with better collaboration with the frontline users, organizations, researchers and global health leaders. There are marked national, regional and local disparities in global NMR due to rural-urban and socioeconomic differences, and heterogeneity in health care coverage. In order to reach the bold international targets of reducing the neonatal mortality, in addition to HBS initiative, programs should focus on reducing geographic disparities and inequality in resource allocation. Though progress has been made in newborn survival, much attention should be paid to the maternal-infant dyad and improve the quality of the maternal care as maternal complications lead to increased neonatal mortality.

Moving towards Every Newborn Action Plan goal of national stillbirth and neonatal mortality rates ≤10 per 1000 births by 2035 will require maturing health systems with adequate infrastructure including access to clean water supply, sanitation and good hygienic practices at delivery. It also requires updated information systems, adequate staffing, training, equipment and transport/referral, as well as an intensified focus on quality of maternal and newborn care (Brizuela & Tuncalp, 2017). In the United States and other developed nations, a person trained and equipped to provide resuscitation at every birth is standard. This has to be the same for the rest of the world.

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

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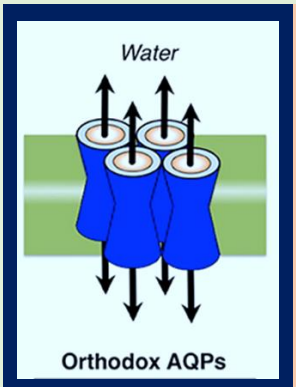

Front Mol Biosci, 18 April 2018, Open Source

Aquaporin Water Channels:

What Are They? What They Do?

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Introduction: About 60% of the human body and 70% of the human brain are nothing but water. The cells in our body are literally filled with water inside and bathe in water outside. Without water, life is not possible. Yet, the water in our body is not like the water inside a vessel. It is compartmentalized in organs, tissues, cells, and vasculature. This compartmentalization needs water-tight barriers and sophisticated regulatory processes for the selective flow of water between the compartments. When these fail, death may ensue as water is no more compartmentalized. Although water can diffuse across cell membranes, it is a very slow process and is affected by factors such as temperature, fluidity of the membrane etc. Transport of water along with ions like sodium via carrier-mediated transport processes can occur. Although, it is a more efficient process than passive diffusion, this piggy backing cannot account for rapid transport of massive amounts of water in certain organs or tissues that happens at all the time in the body. For example, every day, our kidneys filter blood and form about 180 liters of filtrate, enough to fill 2.5 fuel tanks of Ford Explorer. Of this 180 liters of filtered water, 98.9% is reabsorbed back into the blood, eliminating about 1.98 liters per day in the urine. If the fractional reabsorption falls down by less than 1% to 97.8%, the amount of water excreted in the urine will be 3.86 liters per day, which is considered as polyuria. These numbers exemplify how efficient and rapid the movement of water needs to be across some compartments in the body. Based on these and other observations, such as rapid absorption or secretion of fluids in the gastrointestinal tract, mouth, and even in eyes, starting from 1800s, physiologists believed that there must be some "channels" in the cell membranes through which such rapid flow of water can occur in the body. However, it was not until late 1980s, the molecular proof for existence of water channels, now known as the Aquaporins, could be established. This groundbreaking discovery opened a new chapter in the molecular physiology of water homeostasis and pathophysiology of disorders of water balance. Please read the highlight about Peter C. Agre, M.D., who received Nobel Prize in Chemistry for the discovery of Aquaporin water channels in the Pioneers in Medicine and Healthcare section of this issue of Sushruta Medical News. There are several excellent review articles published on the structure, function and pathophysiology of mammalian aquaporins (Verkman AS, 2013; Hu et al, 2013; Zhu et al, 2015; Brown D, 2017; Marinelli et al, 2019; Verkerk et al, 2019; Su et al, 2020; Yadav et al, 2020; Jung et al, 2020; D'Agostino et al, 2020; Bollag et al, 2020; Valenza et al, 2020). The goal of this review is to provide basic information about aquaporins to clinicians so that they can refer to specific publications depending on their interest and specialty.

Aquaporin Water Channels: Aquaporins (AQPs) are a family of membrane proteins widely distributed in mammalian tissues and cells. They are phylogenetically related to each other and share significant degree of sequence homology. They all share some common features, such as molecular weight of about 30 kDa for native non-glycosylated proteins, and six transmembrane regions of the channel protein. As of now, 13 mammalian aquaporins have been reported. They are numbered as 0, 1, 2, 3, 4 etc. AQP0, also known as MIP (Major Integral Protein) of the lens of the eye is like the parent molecule. AQP0 constitutes about 45% of the lens protein, and is essential for establishing refractive index gradient of the lens. Recent studies suggested that AQP0 is involved in the biomechanics of the lens (Kumari et al, 2015). Functionally, all aquaporin channels transport water across cell membranes. They do not determine the direction of the flow. They are just like holes in the membrane. The direction of flow is determined by the osmotic gradients created by active transport of sodium or other ions. While all aquaporins transport water, some, such as AQP3, AQP7, AQP9 and AQP10 also transport glycerol and are known as aquaglyceroporins. They play significant roles in organs or tissues, where transmembrane glycerol transport is crucial, such as adipose tissue, liver, skin, among others. For example, mice genetically lacking AQP3 have reduced skin hydration and elasticity due to impaired transport of glycerol from blood to epidermis. Lack of glycerol also

impairs epidermal proliferation, and glycerol is involved in ATP generation and biosynthesis of membrane lipids. This finding led to spurious claims by certain cosmetic manufacturers that their products stimulate AQP3 (Verkman AS, 2008). Interestingly, aquaglyceroporins also transport metals such as arsenic and antimony. At the physiological pH, these trivalent metals mimic the structure of glycerol, and hence they are able to be transported through aquaglyceroporins. This puts the aquaglyceroporins in the detoxification system of the body (Bhattarcharjee et al, 2009). Some aquaporins, such as AQP1 and AQP4 are blocked by mercury. AQP1 is expressed heavily in the proximal tubular cells of the kidney, where bulk of filtered water is absorbed passively following active reabsorption of sodium. Blocking of AQP1 by mercury results massive loss of water in the urine. This explains the mechanism of mercurial diuretics.

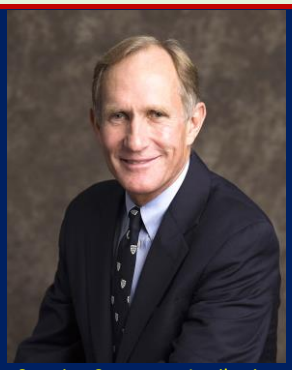
Cellular Distribution and Functional Significance of Mammalian Aquaporins: Thanks to the availability of powerful molecular tools, such as RT-PCR, in situ hybridization to detect expression of mRNA, Western blotting or immunocytochemistry or confocal immunofluorescence microscopy for localization of proteins, the cellular distribution of different types of aquaporins were mapped. Using mice in which a particular type of AQP was genetically deleted, the functional significance of each aquaporin was also established. These in turn allowed to link clinical disorders to dysfunction of aquaporins. It is not possible to describe all those in this short review. The following Table provides expression of AQPs in different tissues, and the phenotype of mice in which specific AQP was genetically deleted.

AQP	Cellular Distribution	Phenotype of AQP-null mice
AQP0	Lens of eye	Cataract
AQP1 (CHIP28)	Proximal part of nephron and microvessels in the kidney; Choroid plexus; Ciliary epithelium; Corneal endothelium; Pain-processing C-fibers; Vascular endothelium; Tumor vessels; Red blood cells	Diuresis; Reduced tumor angiogenesis; Reduced intraocular pressure; Reduced CSF secretion; Reduced nociception
AQP2	Renal collecting duct system; Inner ear; Epididymis; Vas deferens; Vagina	Diuresis due to failure to concentrate urine
AQP3	Renal collecting duct; Epidermis; Conjunctiva; Corneal epithelium; Immune cells; Intestinal epithelium; Red blood cells	Diuresis; Dry skin; Reduced growth of skin tumors; Impaired skin wound healing; Impaired regeneration of colonic epithelium; Impaired leukocyte function
AQP4	Astrocytes; Retinal Muller cells; Lacrimal glands; Salivary duct; Inner ear; Olfactory epithelium; Gastric parietal cells; Airways; Renal collecting duct; Placenta; Muscle; Gut epithelium; Glioblastomas	Reduced cytotoxic or increased vasogenic effects; CNS edema; Accelerated obstructive hydrocephalous; Increased seizure threshold and duration; Deafness; Anosmia
AQP5	Corneal epithelium; Sweat glands; Lacrimal glands; Salivary glands; Airway submucosal glands; Alveolar type I cells; Epidermis	Reduced salivary secretions; Reduced airway submucosal secretions; Thin cornea; Reduced volume of tears
AQP6	Intracellular vesicles in renal collecting duct intercalated cells	None reported
AQP7	Fat cells; Renal proximal tubule (S3); Testis; Myocardium	Obesity; Insulin resistance; Hyperglyceroluria
AQP8	Intestinal epithelium	No major abnormality
AQP9	Hepatocytes; Erythrocytes; Possibly some brain cells	Hyperglycerolemia; Reduced red blood cell glycerol permeability
AQP10	Intestinal enterochromaffin cells	Aqp10 is reported a pseudogene in mice
AQP11	Liver; Testis; Intracellular membranes in renal proximal tubules	Polycystic kidney; Hepatocyte vacuolization
AQP12	Exocrine pancreas	No major abnormality

Conclusion: Thirty years after their discovery, we are still deciphering the functions of different types of aquaporins and trying to understand their pathophysiological roles, mostly depending on genetically modified mouse models. While deletion of certain aquaporins produced clearly evident pathophysiology in mouse models, which correspond to known diseases in humans, the others are not clear yet. This may be due to expression of more than one type of aquaporin in the same tissue or cells.

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

Disclosure: Author declared no competing interests.



Pioneers in Medicine and Healthcare

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Johns Hopkins Bloomberg School of Public Health

Co-Winner of Nobel Prize in Chemistry 2003

Contributed by: Bellamkonda K. Kishore, M.D.

Chance Favors the Prepared Mind – Louis Pasteur

It was late 1980s. Venue, Johns Hopkins School of Medicine in Baltimore, Maryland. **Peter Courtland Agre, M.D**., a Hematologist by training and a Professor of Medicine and Biological Chemistry, was stuck with an unusual finding. Sitting in his office, once occupied by Dr. Albert L. Lehninger, the legendary biochemist, Dr. Agre was deeply contemplating. He had a gut feeling that he stepped on something phenomenal. But little did he realize that he was going to come up with a groundbreaking discovery in biology and medicine. As a hematologist, his interest was studying rare blood group proteins. His lab was extracting proteins from human red blood cell membranes and separating them on polyacrylamide gels. They were consistently finding a particular band of about 28 kDa size showing up in the gels. What was bothering Dr. Agre, this unknown protein constituted 4% of the total membrane proteins, which was high, unless it has a major functional significance. Being a researcher of persistent nature, Dr. Agre kept on probing it further. His lab isolated this protein in pure form, and derived its corresponding cDNA from bone marrow by RT-PCR using degenerate primers. They hypothesized that it must be a membrane channel transporting water and/or other molecules, because red blood cells are know to be resistant to rapid changes in osmolality while passing through different tissues. Experiments on Xenopus (frog) oocytes where they injected cRNA for the protein brought out the Eureka moment. Dr. Peter Agre and his group discovered and cloned the first water channel. Dr. Agre named it as CHIP28 (Channel Forming Intergral Protein of 28 kDa), now called Aquaporin-1. The rest was history. Now we know a whole family of aquaporin water channels in mammals. We also know corresponding water channel molecules in bacteria, algae, and plants. Not only that the discovery and characterization of aquaporin water channels made it possible to understand the physiology of water homeostasis and pathophysiology of disorders of water balance. In some cases, these enabled designing of rational approaches to correct or treat disorders of water balance. Our understanding of water as a biological element essential for life is made possible due to the discovery of aquaporins and the ensuing molecular physiology of water homeostasis (see the article on Aquaporins in this issue for more details).

In recognition of his groundbreaking dicovery, in 2003 Dr. Peter Agre shared Nobel Prize in Chemistry with Dr. Roderick McKinnon for their contribuons on ion and water channels. Dr. Agre is a person who does not rest with a Nobel Prize. His commitment for science, medicine and humanity is unlimited. After receiving the Nobel Prize he served as the President of the American Association for the Advancement of Science (AAAS). During that period he initiated **Science Diplomacy** and toured countries like North Korea and Cuba, where government diplomates are not allowed. Dr. Agre was received by the heads of states and scientific community of those totalitarian regimens with warmth and friendship due to his commitment to sciencce and humanity. Dr. Agre believes that science can unite countries where governments could not.

After his tenure at the AAAS, Dr. Agre returned to the Johns Hopkins Bloomberg School of Public Health as the Director of Malaria Research Institute. One in every two persons ever contacted malaria dies due to the disease. Dr. Agre believes that the solution for malaria eradication lies in understanding the biology and vulnerability of the mosquito, the malaria vector. So, his lab is currently studying the biology of female Anopheles mosquitoes. Sooner or later, they may come up with another major discovery on how to break the connection between the malarial parasite and the human beings by neutralizing the vectors. Such is the caliber, dedication and commitment on the part of Dr. Peter Agre. I was fortunate to collaborate and co-author a publication with this outstanding scientist and exceptional human being while I was working at the National Heart, Lung and Blood Institute in 1990s (Pallone et al, 1997). Please watch the following video clips.

Peter Agre at TEDMED 2011 https://www.youtube.com/watch?v=-eq5tfU1kZY
The Human Side of a Life in Science at TEDxMidAtlantic https://www.youtube.com/watch?v=x4LP9m98obw

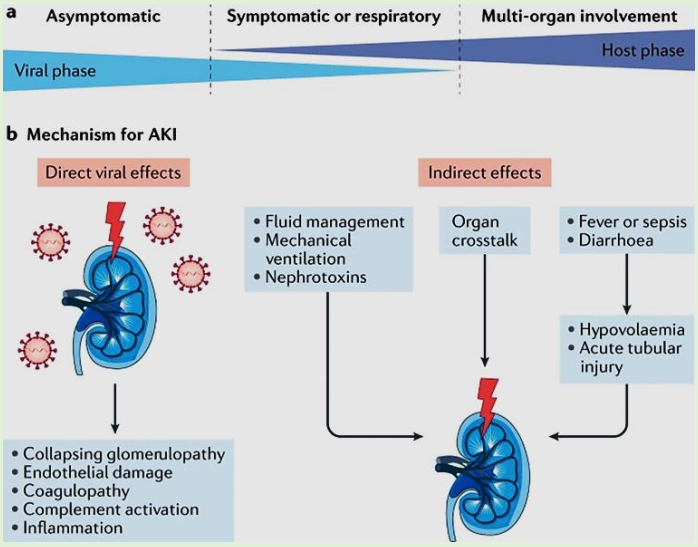
COVID-19-associated Acute Kidney Injury:

Consensus Report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup

Mitra K. Nadim, Lui G. Forni, John A. Kellum

Nature Reviews Nephrology 16: 747–764, 2020

Abstract: Kidney involvement in patients with coronavirus disease 2019 (COVID-19) is common, and can range from the presence of proteinuria and haematuria to acute kidney injury (AKI) requiring renal replacement therapy (RRT; also known as kidney replacement therapy). COVID-19-associated AKI (COVID-19 AKI) is associated with high mortality and serves as an independent risk factor for all-cause in-hospital death in patients with COVID-19. The pathophysiology and mechanisms of AKI in patients with COVID-19 have not been fully elucidated and seem to be multifactorial, in keeping with the pathophysiology of AKI in other patients who are critically ill. Little is known about the prevention and management of COVID-19 AKI. The emergence of regional 'surges' in COVID-19 cases can limit hospital resources, including dialysis availability and supplies; thus, careful daily assessment of available resources is needed. In this Consensus Statement, the Acute Disease Quality Initiative provides recommendations for the diagnosis, prevention and management of COVID-19 AKI based on current literature. We also make recommendations for areas of future research, which are aimed at improving understanding of the underlying processes and improving outcomes for patients with COVID-19 AKI.



a,**b** | **The pathogenesis of AKI in patients with COVID-19 (COVID-19 AKI)** is likely multifactorial, involving both the direct effects of the SARS-CoV-2 virus on the kidney and the indirect mechanisms resulting from systemic consequences of viral infection or effects of the virus on distant organs including the lung, in addition to mechanisms relating to the management of COVID-19. AKI, acute kidney injury. Adapted from Acute Disease Quality Initiative 25, www.ADQI.org, CC BY 2.0 (https://creativecommons.org/licenses/by/2.0/).

COVID-19 and Diabetes

ADA + META: From the American Diabetes Association

META is a Biomedical Research Discovery Tool that analyzes & connects millions of scientific outputs to give us a comprehensive view of how your field is evolving. Through its customizable feeds, we can easily follow developments, intersections, and emerging trends in science. The following publications using Meta-analysis were indexed by the American Diabetes Association. **Click on the journal names to access the websites of the publications**.

COVID-19 Hospitalization in Adults with Type 1 Diabetes: Results from the T1D Exchange Multi-Center Surveillance Study
O'Malley et al, J Clin Endocrin Metab, Nov 2020

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