Universal Health Organisation (UHO) Weekly Newsletter – 15 Dec 2023

The weekly newsletters bring the updates on the science, battered and bruised during the pandemic, legal updates and impact of activism for a just society, across the world. These are small steps to promote Transparency, Empowerment and Accountability – the ethos of the UHO.

Announcement: Membership & endorsements to the UHO invited: https://uho.org.in/member.php

Gene Therapies approved for sickle cell disease in the USA

Sickle cell disease is a genetic disorder in which the shape of the red blood cells which carry oxygen to all organs is shaped like a sickle. The abnormal shape of the red cells makes them vulnerable to destruction by the spleen and liver giving rise to enlargement of these organs. The destructions of the defective red cells also give rise to anemia resulting in lack of adequate oxygen supply to the patient's cells and tissues.

Sickle cell anemia is more prevalent among patients whose ancestors hail from regions which had very high malaria transmission. The sickle shaped Red Blood Cells (RBCs) are resistant to infestation by the malaria parasites. Those with the sickle cell disease had a survival advantage over those with normal RBCs which got infected by the malaria parasite. According to Darwin's law of natural selection by survival of the fittest the people with the abnormal red blood cells were "fit" for survival and the proportion of people carrying the gene for the disease increased in such populations. India with a long history of intense malaria transmission in tribal belts has large pockets of sickle cell disease.

Unfortunately this genetic predisposition which helped some to survive during malaria epidemics is a handicap in normal times. Those born with the sickle cell disease face a multitude of health issues which can vary in severity and presentation among individuals. Recurrent episodes of severe pain due to blocking of blood vessels resulting from debris of the abnormal RBCs are the hallmark of the condition. It can lead to cutting off of the blood supply to different parts and organs and can be life-threatening. The destruction of RBCs also leads to anemia. The patients are also vulnerable to different infections as a consequence of impaired immunity. Children suffering from the condition have stunted growth.

Conventional treatment for this condition is cumbersome and lifelong. It is directed to alleviate symptoms, prevent complications and improve the quality of life. Acute pain is managed by pain relieved medications controlled by the patient. It may also involve hydrotherapy, relaxation and distraction techniques.

Adequate water intake is important to prevent clogging of the vessels due to clumped RBCs. The patient may need repeated blood transfusions. More drastic measures under consideration are stem cell transplant which replaces the bone marrow producing defective cells with stem cells from a healthy donor.

Latest in the fray for curing this so far incurable condition is gene therapy. The US Food and Drug Administration (FDA), recently approved gene therapy for sickle cell disease. This is based on the Nobel Prize winning CRISPR gene editing technology. The gene therapies are approved for patients over 12 years of age. The therapy is based on the principle of "scissoring" away faulty parts of the gene causing sickle cell disease or by introducing modified genes into the body using disabled viruses as carriers. In separate trials both these gene therapies helped reduce painful episodes.

While this development offers some hope for patients suffering from this painful and debilitating condition which shortens their life span, there are some concerns. While the manufacturers of the gene therapies for sickle cell disease, CRISPR Therapeutics and Vertex Pharmaceuticals, have put forward that this is a onetime treatment, data on long term efficacy is limited. The only long term treatment of this condition is a

bone marrow transplant. Treatment with gene therapies can take several months of hospitalization and use of chemotherapy with potential risk of infertility.

The FDA has issued a warning on the potential of developing blood cancer with gene therapy. A couple of years ago, trials involving gene therapy for sickle cell disease were halted after two patients developed cancer.

Gina Smith, in her book, The Genomics Age has said, "Probably no DNA science is at once as hopeful, controversial, hyped, and even as potentially dangerous as the discipline known as gene therapy."

On a lighter note, there is an old saying among magicians that it is important to learn to make things reappear before one should try to make them disappear. Gene therapists should heed this caution. For this more research is needed. Large scale rollout in unholy haste as happened with the gene based Covid vaccines which promised more but delivered less along with concerns of adverse effects like myocarditis should be avoided. Gene therapy may eventually become the therapy of the future. But we have miles to go and should observe the "cautionary tale of scientific overreach." A recent article in Nature has conceded that gene technology needs fine tuning to eliminate unwanted adverse events before they can be rolled out for control of diseases in the future.

According to Siddhartha Mukerjee, the author of The Gene , it would take another decade or so and a lot of learning, for the science of gene therapy to become a reality.

We can only hope that the large tribal population of India, a vulnerable group according to ICMR ethical guidelines, with high prevalence of the sickle cell disease does not become the Petri-dish for gene experiments like it happened with the HPV Vaccine trials in which some tribal girls died.

HPV Vaccine poised to be included in the Universal Immunization Program?

For some time there is lobbying to include the HPV vaccine against cervical cancer in the government's universal immunization program (UIP). A recent news feature in the Times of India mentions a study showing that HPV vaccine is protective even if the first dose is given to girls 15-18 years of age.

While UHO will welcome any vaccine which is safe and effective against cervical cancer it has concerns on including HPV vaccine in the UIP both on scientific and economic grounds.

Cervical cancer is associated with poor genital hygiene, early age of marriage, repeated pregnancies, and multiple sexual partners. The human papillomavirus or HPV is supposed to contribute to precancerous lesions which may progress to cancer.

The majority of HPV infections is asymptomatic and resolve spontaneously. The prevalence of HPV infection in countries varies – ranging from 2% to 42%. Women living with AIDS have a much higher prevalence, around 54%

At the individual level, prevention is cheaper than cure if one follows a healthy lifestyle, including safe sex and genital hygiene in the context of cervical cancer. Mass vaccination without strong evidence of efficacy is not cheaper than cure. Countries may spend a huge amount of taxpayer money on vaccines for all where only a minority may be at risk. For vaccine manufacturers, newer vaccines are like 'Mackenna's Gold'.

Scientific papers without any conflicts of interest or funding from the pharma industry have expressed serious doubts about the efficacy of HPV vaccines in preventing cervical cancer. One such paper titled,

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PEOPLE'S HEALTH IN PEOPLE'S HANDS

'Will HPV vaccination prevent cervical cancer?' published in the Journal of Royal Society of Medicine, critically reviews the efficacy of HPV vaccines, and concludes that there could be multiple methodological problems with the trials. The paper states that the trials were not designed to detect protection against the outcome i.e. cancer which take many years to develop. Follow up was limited to 4-5 years. While vaccines may prevent very early pre-cancer lesions, most of these could be self-limiting. Prevention of these surrogate endpoints may not confirm the efficacy. Most trials reported relative risk, which overstates the efficacy instead of the attributable risk which is marginal.

While the jury is out, a recent paper published on BMC's website revealed that incidence and deaths from cervical cancer over the last three decades have fallen drastically in the country, in spite of which advocates of the vaccine keep parroting "it is still a major public health problem in India." By synchronizing this natural ly falling trend with inclusion of HPV vaccine in the UIP vested interests can easily convince the gullible people of the positive impact of this infructuous intervention at great cost to the exchequer.

Given the gaps in evidence, UHO states that evidence does not support the inclusion of the HPV vaccine in the UIP. It would be a wasteful expenditure of public funds with uncertain benefits. Moreover, mass vaccination could go on to eliminate the control group of unvaccinated women to resolve some of the uncertainties of the efficacy of HPV vaccines.

As cervical cancer takes decades to develop, we need to follow up both vaccinated and unvaccinated groups into their 40s and above to ascertain the benefit and harms, if any.

Sudden deaths mostly due to heart attacks up 12% in 2022 in the country

Sudden deaths claimed 56, 653 lives in India in 2022 a rise of 12% above baseline levels according to the National Crime Records Bureau (NCRB). Most of these deaths were due to heart attacks. Majority of the sudden deaths occurred in men mostly below 60 years.

Hard data like these should be taken seriously and properly investigated in an objective and scientific manner. Instead the ICMR appears to be involved in a cover up operations. It published a couple of shoddy studies showing no correlation of the Covid-19 vaccines with such unusual incidents which was pointed out earlier also.

As a watchdog of people's health and safety, UHO advocates for transparency and honesty on part of ICMR, empowerment of the people to ask for confirmation of cause of such sudden deaths based on the totality of evidence, such as robust randomized controlled trials, cohort studies and backed with post-mortem studies, including histopathology and biochemical markers. At stake are human lives.