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## Editing Gene to Prevent Inheritable Disease

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New Hope for  
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# Scientific European®

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### NOTE FROM THE FOUNDER & EDITOR-IN-CHIEF

We always thought there was a greater need to bring cutting edge relevant scientific advances to general audience across the globe for their appreciation because at the end of the day science must serve society and intellectual stimulation of the people has the potential to further advance science itself.

The idea to launch a popular science magazine titled Scientific European arose out of my discussion with Cambridge alumnus molecular biologist Dr Rajeev Soni and here we are with the maiden issue of Scientific European (SCIEU).

With immense pleasure, we bring to you hugely relevant recent scientific advances on six key themes, compiled and presented by my colleague and I.

With this we embark on the eternal journey to bring scientific advances to the living rooms of the people across the world.

Umesh Prasad

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# The Possible Cure of Type 2 Diabetes?

JASMITA GILL

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*The Lancet study shows that Type 2 diabetes can be reversed in adult patients by following a rigorous weight management programme.*

Type 2 diabetes is the most common type of diabetes and is looked as a chronic progressive disease which requires lifelong medical treatment. The number of people with type 2 diabetes has quadrupled over the past 35 years worldwide, and this number is expected to cross 600 million by 2040. This study shows that increase in type 2 diabetes patients is linked to the alarming rise in levels of obesity and the accumulation of fat in the abdomen.

*Healthier lifestyle as an alternative to anti-diabetic drugs?*

It has been discoursed many times that type 2 diabetes may be reversible or even completely cut out with a timely combination of healthier diet, physical activity and lifestyle changes. In short, a lifestyle overhaul. Also, it has been established that being overweight (BMI greater than 25) increases risk of developing type 2 diabetes. However, the focus has mainly remained on prescribing drug treatments to reduce blood sugar levels. Diet and lifestyle changes are elaborately discussed but generally these therapies do not include cutting calories or substantial weight loss. In short, the root cause has never been pondered upon.

*Lifestyle overhaul*

So, what can be done to reverse the incidence of type 2 diabetes? The recent study in Lancet<sup>1</sup> shows that a complete lifestyle overhaul is the key factor in controlling this disease. The study analyses and builds up on the underlying cause of the condition, leading to interesting outcomes. It has been shown that after 1 year, participants had lost an average of 10kg, and nearly half of them had reverted to a non-diabetic state while not using any form of treatment for diabetes. This study led by Professor Roy Taylor, from Newcastle University, and Professor Mike Lean from Glasgow University, is novel in the aspect of advising dietary weight loss to participants but with no noteworthy increase in physical activity. However, the long-term follow ups definitely require sustained daily activity.

The Diabetes Remission Clinical Trial (DiRECT) included 298 adults aged 20-65 years who had been diagnosed with type 2 diabetes in the past 6 years. Here, the authors do note that the majority of the participants were British white, conveying that their findings may not broadly apply to other ethnic groups.

## *Cutting calories is the key*

The weight management programme was delivered by dieticians and/or nurses and began with a diet replacement phase consisting of a low-calorie formula diet. The calorie controlled diet involved a daily maximum limit of 825-853 calories per day, for about three to five months. This was followed by graded reintroduction of certain other foods. These dietary regulations were combined with cognitive behaviour therapy sessions and some form of exercise to support continuous weight loss maintenance. All Antidiabetic medications were stopped at the start of the programme.

A previous study<sup>2</sup> by the same researchers had confirmed the Twin Cycle Hypothesis which stated that a major cause of type 2 diabetes is the excess fat within the liver and pancreas. They had established that people with the disease can be returned to normal glucose control by consuming and maintaining a very low-calorie diet thus allowing these organs to return to normal function.

## *Remission of type 2 diabetes as the principal outcome*

The principal outcomes of the intensive weight management programme were weight loss of 15 kg or more, substantially improved quality of life at 12 months and most importantly remission of diabetes. Significant improvement was also noted in the average blood lipid concentrations and almost 50 percent of patients did not show any rise in blood pressure, thus not requiring any antihypertensive drugs.

This finding is very exciting and remarkable, and could revolutionize the treatment of type 2 diabetes. It also indicated that the very large weight losses targeted by bariatric surgery (risk, unsuitability to most patients) may not be a necessity and a very comparable objective of weight loss which such a programme provides is a more reasonable and practically achievable proposition for many patients and will regular follow ups. Intensive weight loss (which could be provided in a non-specialist community setting) is not only linked to better management of type 2 diabetes but also could result in lasting remission.

## *Challenges ahead*

This study paves way for strategies for prevention and early care of type 2 diabetes as the primary goal. Putting Type 2 diabetes into remission as early as possible after diagnosis can have extraordinary benefits and as the study shows, it may well be possible for almost half of all patients to achieve this in routine primary care setting and without drugs.

However, the methodology described may not likely be a way which can be sustainable for life as it is not easy and its very challenging for people to live on a prescribed formula diet for their "entire life". Hence, the obvious big challenge for this methodology is the long-term avoidance of weight re-gain. No doubt, that flexibility needs to be encouraged to optimize individual results. Further, correct behavioral interventions and programs that encourage and support the patients to instinctively carry out lifestyle changes need to be designed. This shall require both individual-level and also wider strategies including economic decision like taxation of unhealthy foods.

The findings published in Lancet propagates extensive use of intensive weight loss intervention strategies in the routine care and remission of type 2 diabetes in the health sector.

Source:

1. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. Lean, Michael EJ et al. The Lancet DOI: [http://dx.doi.org/10.1016/S0140-6736\(17\)33102-1](http://dx.doi.org/10.1016/S0140-6736(17)33102-1)
2. Taylor, Roy. Type 2 diabetes: Etiology and reversibility. Diabetes Care, April 2013, vol. 36, no. 4, pp:1047-1055.



# New Hope For People Needing Organ Transplant

UMESH PRASAD

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## *First study to show development of interspecies chimera*

In a study published in *Cell*<sup>1</sup>, chimeras - named after the mythical lion-goat-serpent monster – are made for the first time by combining material from human and animals. The human cells can be successfully seen growing inside a pig after human stem cells (which have the capability develop into any tissue) are injected into the pig embryo by a cutting-edge stem cell technology.

This study led by Professor Juan Carlos Izpisua Belmonte at Salk Institute for Biological Studies in California is a huge breakthrough and pioneer work in understanding and realizing the potential of interspecies chimeras and provides unprecedented ability to study early embryo development and organ formation.

## *How is the human-pig chimera developed?*

However, the authors describe this process as fairly inefficient with low success rate of only ~9 percent but they also observed that human cells were seen successfully functioning when part of a human-pig chimera. The low success rate is mainly attributed to the evolutionary gaps between human and pig and also there was no evidence that human cells were integrating into the premature form of brain tissue. The low success rate notwithstanding, the observations show that billions of cells in the chimera embryo would still have millions of human cells. The testing of these cells alone (even 0.1% to 1%) would certainly be meaningful in a larger context to achieve long term understanding of interspecies chimera.

A related chimera study was also published around the same time in *Nature* led by Hiromitsu Nakauchi at Stanford Institute for Stem Cell Biology and Regenerative Medicine that reports functional islets in rat-mouse chimeras<sup>2</sup>.

## *Ethical discussion around chimeras, how far can we go?*

However, the studies related to development of interspecies chimeras is also ethically debatable and raises concerns about to what extent such studies can be done and is legally and socially acceptable. This involves ethically responsibility and legal decision-making bodies and also raises several questions.

If we take into account all ethical considerations, it is uncertain if a human-animal chimera can be ever born. Will it be ethical if its born but not allowed breed by making it sterile? Also, how much percentage of human brain cells can be part of chimera is also questionable. Could the chimera potentially fall into some uncomfortable gray area as a subject in between of animal and human research. Scientists don't know much about their own species because of the many barriers to research on humans. These barriers include no support for embryo research, prohibition of any clinical trials related to germline (cells that become sperm or eggs) genetic modification and limitations on the human developmental biology research.

No doubt, scientists will have to tackle these questions at an appropriate time rather than avoiding them. Such efforts will provide a foundation and advance the way for further research which is ethically sound and provide deeper insights into "being human".

The authors categorically state that their objective is to primarily understand how cells of two different species (pig and human here) mix, differentiate and integrate and that they have analyzed the human-pig chimera at a very early stage in development.

## *Multiple challenges but immense hope for the future*

This study is exciting despite being ethically challenging and marks the first step toward generating transplantable human organs using large animals (pig, cow etc.) whose organ size and physiology is very close and similar to humans. However, if we look at the current study, the levels of immune rejection are very high as we speak. The pig contributions (cells from pig) into every organ that grows in the chimera is an extremely big challenge for any thoughts about successful organ transplantation into humans.

Nevertheless, the real hope for the future here is to be able to have a **new source of organs for transplants** in humans by using stem-cell and gene-editing technologies. This is important and the need of the hour, given the enormous need for transplant amongst patients, many of whom die on the waiting list (especially with kidney and liver requirements) and also the huge lack of enough donors.

Authors assert that this study shall impact other related areas of research as well. The continued development of chimeras with relatively more human tissue has implications and usefulness in studying onset of diseases in humans and for screening drugs before trials on human participants apart from understanding the differences between the species. In this study, the technology was not used for human chimeras, but theoretically speaking a complementary methodology could be devised in the future in trying to use chimeras to make human organs for transplantation. More work in this area shall throw insights on the possible success and limitations of these technologies when used to develop chimera.

This is a first and crucial study on the development of human and animal chimeras and paves way to further the scientific community's understanding of the creation and development paths of cells in an animal setting.

Source:

1. Interspecies Chimerism with Mammalian Pluripotent Stem Cells. Wu, Jun et al. Cell, Volume 168, Issue 3, 473 - 486. e15. doi: <http://dx.doi.org/10.1016/j.cell.2016.12.036>
2. Interspecies organogenesis generates autologous functional islets. Tomoyuki Yamaguchi, Hideyuki Sato, Megumi Kato-Itoh, Teppei Goto, Hiromasa Hara, Makoto Sanbo, Naoaki Mizuno, Toshihiro Kobayashi, Ayaka Yanagida, Ayumi Umino, Yasunori Ota, Sanae Hamanaka, Hideki Masaki, Sheikh Tamir Rashid, Masumi Hirabayashi & Hiromitsu Nakauchi Nature 542, 191–196. doi:10.1038/nature21070



# Editing Gene to Prevent Inheritable Disease

JASMITA GILL

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## *Study shows gene editing technique to protect one's descendants from inheritable diseases*

The study published in *Nature* has shown for the first time that a human embryo can be corrected at a very early stage of embryonic development by a gene-editing technique called CRISPR. The study, a collaboration between the Salk Institute, Oregon Health and Science University in Portland and Institute for Basic Science in Korea show that researchers have corrected pathogenic gene mutation for a heart condition in the human embryo so as to eliminate this disease in the present offspring and future generations. The study provides significant insights into preventing thousands of diseases that are caused by single/multiple mutations in only one gene.

## *Correcting disease-related single gene before beginning of life*

A heart condition called Hypertrophic cardiomyopathy (HCM) is the most common cause of sudden cardiac arrest leading to death and affects approximately 1 in 500 people of any age or gender. HCM is thought to be the most common inherited or genetic heart condition worldwide. It is caused by a dominant mutation in a gene (MYBPC3) but the presence of this condition is not detected until it is too late. People with a mutant copy of this gene have a 50 percent chance of passing it on to their own children and thus correcting this mutation in embryos would prevent the disease not only in affected children, but also in their future descendants. Using IVF (In vitro fertilization) techniques, the researchers injected the corrected gene components into healthy donor eggs fertilized with the donor's sperm. Their methodology allows the donor's cells' own DNA-repair mechanisms to correct the mutation during the next round of cell division. The mutation is basically corrected by using either an artificial DNA sequence or the non-mutated copy of original MYBPC3 gene as a starting template.

They then analyzed all the cells in the early embryos to see how effectively the mutation was repaired. The technique of gene editing though at a very preliminary stage in the current study, has been found to be safe, accurate and effective. In short basically "it's working". It was surprising for the researchers to see that the gene editing went off very well and they did not see any side concerns like induction of detectable off-target mutations and/or genome instability. They have developed a robust strategy to ensure consistent repair in all the cells of the embryo. This is a novel strategy (though very "preliminary" in the words of the authors) which has not been reported so far and this technology successfully repairs the disease-causing single gene mutation by taking advantage of a DNA repair response which is very unique to embryos only at a very early stage of conception.

# *Ethical debate around gene editing*

Such advances in stem cell technologies and gene editing -though still very much in infancy - have given hope to possibly millions of people inheriting disease-causing mutations in their genes by showing a technique to prevent and cure a number of such diseases. The potential of this study is huge and impactful; however, this is an ethically debatable topic and any steps towards such studies have to be cautiously taken by after giving highest consideration to all necessary ethical judgments. Other barriers to this type of study include no support for embryo research and prohibition of any clinical trials related to germline (cells that become sperm or eggs) genetic modification. One instance which the researchers have categorically stated is careful avoidance of introduction of unintended mutations into the germ line.

The authors have stated that their study is fully compliant with the recommendations in the 2016 roadmap "Human Genome Editing: Science, Ethics, and Governance" by the National Academy of Sciences, USA.

## *Making a huge impact with possibilities*

The results of this study in Nature demonstrate the great potential of embryonic gene editing. This is the first and the largest study in the area of gene editing. However, this area of research is encumbered with realistic assessment of both benefits and the risks along with a continuous assessment of the safety and efficacy of the procedure in a broader perspective.

On an optimistic note, this research shall have a huge impact on discovering eventual cures for thousands of diseases which are caused by mutations in single genes. In a "very distant future", these edited embryos could be transplanted into a uterus with the goal of establishing a pregnancy and during such a process, a clinical trial could then monitor the embryos as they develop into offspring. It sounds farfetched at this moment, but that is the intended long-term goal of this study. The groundwork has been made by bringing scientists one step closer to snipping inherited genetic diseases out of human offspring.

Source:

Hong Ma, Nuria Marti-Gutierrez, Sang-Wook Park, Jun Wu, Yeonmi Lee, Keiichiro Suzuki, Amy Koski, Dongmei Ji, Tomonari Hayama, Riffat Ahmed, Hayley Darby, Crystal Van Dyken, Ying Li, Eunju Kang, A.-Reum Park, Daesik Kim, Sang-Tae Kim, Jianhui Gong, Ying Gu, Xun Xu, David Battaglia, Sacha A. Krieg, David M. Lee, Diana H. Wu, Don P. Wolf, Stephen B. Heitner, Juan Carlos Izpisua Belmonte, Paula Amato, Jin-Soo Kim, Sanjiv Kaul, Shoukhrat Mitalipov. Correction of a pathogenic gene mutation in human embryos. Nature, 2017; DOI: 10.1038/nature23305



# “Moderation” Approach to Nutrition Reduces Health Risks

UMESH PRASAD

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*Multiple Studies shows that moderate intake of different dietary constituents is best associated with lower risk of death*

Researchers have formulated data from a major global study - Prospective Urban Rural Epidemiology (PURE) study<sup>1</sup> to analyze the relationship between nutrition and disease. They followed around 135,000 participants from 18 countries (low-income, middle-income and high-income) across five continents. The study took note of people's diet and did a follow up on them for an average of 7.4 years.

The study found that high carbohydrate intake was associated with an increased risk of death. In popular belief, it has always been discussed that consuming a higher amount of dietary fats (saturated fats, polyunsaturated fats and mono unsaturated fats) is associated with a lower risk of death when compared to lower intakes. Though, total or individual fats were not associated with risk of heart attacks or any major type of cardiovascular disease. However, on the other hand, the study also found that a diet that is high in carbohydrates is related to higher mortality though with lower risk of cardiovascular disease.

It would not be an exaggeration to state that this study in *Lancet* definitely questions the conventional beliefs and opinions about dietary fats and their respective clinical outcomes. The results of the study might appear “surprising” as they show a very different picture of possibilities when it is viewed in context with previous studies. These thoughts notwithstanding, the researchers clarify that these new results are very much consistent with several studies and randomized trials that have been conducted in developed countries during the last two decades or so.

In developing countries (of South Asia particularly), the study found that any decrease in dietary fat intake automatically led to increased consumption of carbohydrate. The researchers explain that this increase in carbohydrates but not fat was contributing to higher mortality rates in South Asia.

It is interesting to note that dietary guidelines around the globe have mainly focused on reducing the overall daily fat to below at least 30 per cent of daily caloric intake and saturated fat to

below 10 per cent of caloric intake. This has been based on the knowledge that reduction of fat (particularly saturated fat) should lessen the risk of cardiovascular disease. These guidelines were developed more than 40 years ago and since then the overall consumption of fat has also fallen in western countries. However, the authors point out that these learnings and guidelines previously reported did not always take into account how the saturated fats are being replaced in the diet which is obviously heavily influenced by geographical location and also social and cultural demography.

Another related PURE report concurrently published in *Lancet*<sup>2</sup> assessed the global consumption of fruit, vegetable and legume and its relation to mortality and heart attacks and diseases. While the study found a beneficial effect of increasing consumption of fruit, vegetables, and legumes, the maximum benefit was seen at three to four servings a day (or a total of 375–500 grams) especially when eaten raw than cooked and with no additional benefit from consuming more. This acquired relevance since vegetables and especially fruits are an expensive food item and thus unaffordable to the larger population in the regions of Asia and Africa. Thus, a target of minimum three servings in a day sounds achievable and affordable. This is thought-provoking since most dietary guidelines have always recommended a minimum of five daily servings and also did not differentiate between the benefits of raw vs cooked vegetables. The authors point out that the studies which credited five daily servings of fruits and vegetables for decreased risk of cardiovascular diseases, were carried out mainly in developed countries.

Legumes including beans, peas, lentils, chickpeas etc. are routinely consumed by many populations in South Asia, Africa and South America. It has been found that eating just one daily serving definitely decreases the risk of cardiovascular disease and death. Since legumes are not popularly consumed in Europe or North America, replacing starches like pasta or white bread with more legumes would be a promising dietary transformation in developed countries.

A final third study in *The Lancet Diabetes and Endocrinology*<sup>3</sup> by the same group of researchers examined the impact of fats and carbohydrates on blood lipids and blood pressure. They found that LDL (so-called 'bad' cholesterol) is not reliable in forecasting the effects of saturated fat on future cardiovascular events. Instead, the ratio of 2 organizing proteins (ApoB and ApoA1) in the blood offer best indication of the impact of saturated fat on cardiovascular risk on the patient.

The PURE study has included populations from varied geographic regions which have not been studied before (especially South Asia and Africa) and the diversity of populations evaluated in this study strengthens the data on foods which potentially reduce disease risk. The authors emphasize that "moderation" in most aspects of diet should be the preferred approach, as opposed to the popular notions of having very low or very high intakes of most nutrients. The idea of "moderation" becomes extremely relevant since nutritional inadequacy is a bigger challenge in developing countries when compared to nutritional excesses in developed countries. The findings in this study are globally applicable and has the potential propose a "reconsideration" of nutrition policies based on socio-economic conditions.

Source:

1. Dehghan, Mahshid & Mente, Andrew & Zhang, Xiaohe & Swaminathan, Sumathi & Li, Wei & Mohan, Viswanathan & Iqbal, Romaina & Kumar, Raj & Wentzel-Viljoen, Edelweiss & Rosengren, Annika & Itty Amma, Leela & Avezum, Alvaro & Chifamba, Jephthah & Diaz, Rafael & Khatib, Rasha & Lopez-Jaramillo, Patricio & Liu, Xiaoyun & Gupta, Rajeev & Mapanga, Rudo. (2017). Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): A prospective cohort study. *The Lancet*. DOI:10.1016/S0140-6736(17)32252-3

2. Salim Yusuf, DPhil et al. Fruit, vegetable, and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study. *The Lancet*, August 2017 DOI: 10.1016/S0140-6736(17)32253-5

3. Association of dietary nutrients with blood lipids and blood pressure in 18 countries: a cross-sectional analysis from the PURE study Mente, Andrew Yusuf, S et al. *The Lancet Diabetes & Endocrinology*, Volume 5, Issue 10, 774 – 787. DOI: [https://doi.org/10.1016/S2213-8587\(17\)30283-8](https://doi.org/10.1016/S2213-8587(17)30283-8)



# A Double Whammy: Climate Change is Affecting Air Pollution

JASMITA GILL

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## *Study shows the severe effects of climate change on air pollution thus further impacting mortality worldwide*

A new study has shown that future climate change if left unaddressed, has the potential to cause approximately 60,000 deaths globally by the year 2030 and more than 250,000 deaths in 2100 due to its powerful impact on air pollution.

The study published in *Nature Climate Change* has added to the growing number of reports and evidences pointing at the various negative outcomes of changing climate and that it's high time it is considered a "real phenomena" and not a "myth". This study carried out by Professor Jason West and his team at University of North Carolina at Chapel Hill, USA is also the most comprehensive study on how climate change will have an impact on global health via air pollution because the researchers here have utilized results from several climate change modeling groups worldwide.

## *Ensemble of models used for analysis*

Researchers have used several collaborative global climate models (United States, United Kingdom, France, Japan and New Zealand) to determine the approximate number of premature deaths that would occur in 2030 and 2100 mainly due to ground-level ozone and fine particulate matter (specially PM<sub>2.5</sub>). In all of these models, the researchers assessed the likely changes in ground-level air pollution which could be directly attributed to future overall climate change.

These changes were spatially overlaid onto the global population, thus taking into account population growth as well as the probable changes that point towards increased susceptibility to air pollution. The results of the study show that climate change is expected to cause an increase in air pollution-related deaths globally and in all world regions (with highest in India and East Asia) though Africa was an exemption. It was seen that five out of eight models predicted there will be higher premature deaths worldwide in 2030, and seven of nine models in 2100.

# *Climate change needs to be taken more seriously*

Climate change like rise in global temperatures tend to speed up the chemical reactions that create air pollutants like ozone and fine particulate matter. The geographical locations that get drier with no or minimal rain also show increase in air pollution mainly due to factors like less removal of air pollutants by rain, increased fires and dust. The green cover (trees and grass) also emits comparatively more organic pollutants in hotter temperatures. So basically, climate change strongly affects concentrations of air pollutants impacting air quality and thus impacting overall health. It is a vicious circle and starts with climate change at its origin.

The notoriety of climate change doesn't end here. It is responsible not only for exacerbating air pollution-related deaths, but is also expected to caused in lung disease, heart conditions, and stroke heat stress, scarcity of clean water and food, storms and the spread of infectious diseases thus being a huge burden on public health worldwide. Climate change mitigation is need of the hour and is highly likely to reduce air-pollution-related mortalityworldwide.

Source:

Silva RA, J West J, Lamarque J-F, et al. "Future Global Mortality from Changes in Air Pollution Attributable to Climate Change." *Nature Climate Change* 7, 647–651 (2017). doi:10.1038/nclimate33547



# Artificial Womb: Hope For Millions of Premature Babies

UMESH PRASAD

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*A study has successfully developed and tested an external womb-like vessel on baby sheep, generating hope for premature human babies in the future*

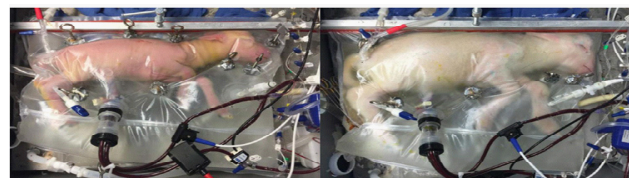
An artificial womb designed and developed with an intent to support fragile premature babies has been successfully demonstrated for the first time ever in animals (baby sheep here). This study published in *Nature Communications* is a major scientific breakthrough for the year 2017 and has generated immense hope for preterm newborns. This is the kind of study that immediately strikes a chord with the general public as it has a huge potential to affect the lives of millions of preterm babies worldwide.

## *Mimicking the womb*

The study led by Professor Alan Flake, a surgeon and director of the Center for Fetal Research in the Center for Fetal Diagnosis and Treatment at Children's Hospital of Philadelphia, USA shows that lambs that are born preterm (at the equivalent of 23 or 24 weeks gestation human infant) were successfully kept alive and also appeared to develop normally while floating inside a transparent, womb-like support container or vessel, called the "Biobag".

This current novel system mimics life in the uterus as closely as possible by utilizing knowledge from previous neonatal research. It uses a distinctive fluid-filled plastic container or vessel attached to other custom-designed machines which provide the necessary physiological support. The fetal lambs grow in a sealed, temperature-controlled, sterile environment insulated from any variations (temperature, pressure or light) and hazardous infections, while breathing amniotic fluid as they normally would do in the womb. The baby's heart pumps blood via the umbilical cord into the system's low-resistance external oxygenator that very intelligently substitutes for the mother's placenta in exchanging oxygen and carbon dioxide. This is extremely necessary since at this gestation period baby's lungs are not developed yet to breathe in oxygen from the atmosphere. Different electronic monitors continuously measure their vital signs. For the system to be successful, its inflow and outflow apparatus have been continuously designed and redesigned at regular intervals. The lambs successfully continued to grow in the Biobag for full four weeks (670 hr over 28 days) after their birth and showed normal breathing, swallowing, eye movement, activity signs, sprouted wool and a very normal growth and organ maturation. Researchers call this as an "awe-inspiring sight" but nevertheless, they state that their system needs continuous evaluation and refinement.

The researchers did not try to extend viability to an earlier period than the current mark of 23 weeks because of several limitations which increase risks, including size, physiological functioning that would impose unacceptably high risks. Most of the lambs from the study were euthanized before they reached full term for further evaluation; however one is now a healthy grown sheep.



## *Premature births: a big burden*

It has been predicted that 15 million human babies are born preterm (before 37 weeks) every year worldwide and this number is only increasing. The rate of preterm birth ranges from 5% to 18% of babies born in 184 countries worldwide. Complications that arise due to preterm birth are a leading cause of death among children below the age of 5.

Majority of infant deaths are attributed to prematurity even after significant improvement in neonatal care practices. And even though fragile infants who are able to survive at 23-23 weeks period (30-50 percent do), they still have to suffer from an inferior quality of life, facing permanent health problems and even lifelong disability in many cases. Also, access to high-level care affects the outcomes differently in each case. These scenarios also put a financial and emotional burden on parents as well as the health sector.

## *Now sheep, next is humans?*

This study tests and monitors the effects on fetal lambs and it is already known that prenatal lung development in sheep is very similar to humans. Though, the sheep brains develop at a somewhat different pace than humans. The current system as it is, needs to be downsized for human infants, who are around one-third the size of the infant lambs that were used in the study. This study though is extremely challenging in humans, will have a huge impact on premature babies. If it is similarly successful for human babies in the coming 1-2 decades, there is an astonishing likelihood that extremely premature infants will continue to develop in chambers or vessels that are filled with womb-like amniotic fluid, rather than relying on incubators supported by ventilators and won't have to suffer from multiple invasive procedures.

Human testing which can be carried forward from this study is still, realistically speaking, a couple of decades away, but this study definitely predicts possible similar success on human infants. The main aim is to cross the threshold of 28 weeks for human premature babies, which then reduces any severe outcomes on life. Such an extra-uterine system/artificial womb if developed for growth and organ maturation for only just a few weeks can still dramatically improve outcomes for premature human babies.

## *This is an appealing, extraordinary science*

Looking at this study, we could start imagining a world where babies can grow in an artificially simulated womb thus eliminating possible health risks of pregnancy which affect the mother as well as the unborn baby. However, we cannot get carried away with these thoughts, because removing the most important element - "the creator and nurturer of life" - the mother from the entire process would really make growth of babies (from 0 till 9 months) a stuff of science fiction with the entire early development happening literally on a machine. The idea which researchers have propagated is not to "entirely eliminate" mothers but rather provide a technology to reduce and/or prevent mortality and morbidity caused by preterm births.

Source:

Partridge EA, Davey MG, Hornick MA, et al (2017) An extra-uterine system to physiologically support the extreme premature lamb. Nature Communications 8:15112. doi:10.1038/ncomms15112.