Controlled Human Infection Studies

Why in news?

Recently, Indian Council of Medical Research (ICMR) released a policy statement for the ethical conduct of Controlled Human Infection Studies (CHIS).

What is controlled human infection studies?

- It refers to the research methodology that involves *intentionally exposing healthy human volunteers to a specific pathogen or infectious agent* under controlled conditions.
- It is also called as human challenge studies in India which is different from human clinical trials.
- **Aim**- To understand disease pathophysiology & immune responses, develop vaccines, test treatment modalities and evaluate the safety and efficiency of potential new chemical entities.
    - Example- The yellow fever study in the early 1900s, for instance, established that mosquitoes transmitted the yellow fever virus.
- **Types**
    - Vaccine development trails
    - Treatment studies
    - Challenge studies

What are the benefits of CHIS?

Infectious disease contributes about 30% of the disease burden in the country.

- **Better insights of disease**- Conducting these studies in endemic settings can lead to outcomes relevant to the local population.
- **Drugs in lesser time** - Vaccine research uses data related to immune responses in early vaccine development and assess the minimum required dose for protection and immunization in shorter time frames.
- **Better medical surveillance**- Researchers can closely monitor the development and progression of an infectious disease from its earliest stages.
- **Effective policy**- CHIS can improve understanding of specific aspects of the transmission patterns this would contribute to the development of effective public health strategies and policies.

- **Improve research capacity**- Conducting CHIS can contribute towards building local research capacities, clinical facilities, laboratory diagnostics, experimental medicine and clinical governance on par with global initiatives.

Many countries, including low-and middle-income countries such as Colombia, Kenya, Tanzania and Thailand, have carried out human challenge studies.

What is the difference between human clinical trials and human challenge studies?

About	Human clinical trials	Human challenge studies
Nature of exposure to pathogens by participants	They are strongly advised to adopt and adhere to safety measures to avoid getting infected.	Volunteers in a human challenge study are deliberately exposed to disease-causing pathogen
Aim	To study the safety and efficacy of drugs and vaccines	To understand the various facets of infection and disease pathogenesis besides selecting the best candidate drug or vaccine
Adverse effects	Safety is evaluated for the first time in humans during the phase-1 stage of a traditional trial	They face an additional risk when deliberately exposed to the pathogen.
Implementation	They are undertaken in four phases generally to test the efficacy.	They are undertaken to study "less deadly diseases" such as influenza, dengue, typhoid, cholera and malaria

- **Special safeguards-** There has been a special safeguard in human challenge studies to prevent from SARS CoV 2 virus that causes COVID
    - To reduce harm to the participants, a *weaker or less virulent* form of the pathogen is used.
    - There should be a *'rescue remedy'* to prevent the disease from progressing to its severe form.
        - Example- *Remdesivir* as rescue remedy for the participants in SARS-CoV-2 virus studies even when the substantial mortality benefit of remdesivir is unknown.

What are the guidelines in ICMR consensus policy statement?

- **Allowed to participate**- It is clearly mentioned that only healthy individuals in the 18-45 years age bracket are to be enrolled.
- **Not allowed to participate-**
    - Children and women who are pregnant, lactating or
    - Planning to conceive within the study period
    - Children will be included when "deemed appropriate"
    - Participants with pre-existing medical conditions.

- **Medical Examination**-A detailed medical examination of the participants is required before enrolment.
- **Payment for participants**- Information on payment should be mentioned in the consent form but the exact amount of payment for participation is to be revealed "only after the volunteer has consented to participate".

What are the ethical issues with human challenge studies?

- **Deliberate exposure-** The human challenge trial are deliberately exposed to a disease-causing pathogen which makes it ethically more challenging.
- **Payment issue-** It is left to the investigators to not reveal the payment before the participant gives his or her informed consent.
- Assured payment even when the amount is not revealed may serve as an inducement.
- **Need of effective rescue remedy** – Infections like SARS-CoV-2 virus remains asymptomatic in some people while leading to death in others.
- The disease state in an individual cannot be 100% predicted even when a less infectious agent is used.
- **Issue with informed consent-** When the pathogen is studied in specific age groups such as children or disadvantaged groups.
    - Example- HPV vaccine trial in Andhra Pradesh in 2010, COVAXIN trial in Bhopal in 2020.

What lies ahead?

- Indian scientists should gain medical intervention expertise knowledge.
- There should be robust institutional structures and mechanisms in place to deal with the ethical challenges of human challenge studies.

References

1. The Hindu| Explained human challenge studies
2. The Hindu| Controlled human infection studies
3. ICMR| Policy statement on human challenge studies