Biomedical Research Methods-II

Pınar Yılgör Huri

Pre-clinical trials

- This involves non-human animal models to help expand our knowledge of more effective methods for diagnosing, treating, and curing diseases that can affect both humans and animals. Researchers use animal models in more advanced levels of biomedical research because animals are biologically similar to humans and are susceptible to many of the same diseases.

Clinical Trials

- These involve human volunteers and take place in a hospital or clinical setting. These trials can take place after the drug/compound has passed safety testing in animals. The human volunteers allow researchers to gauge the effectiveness and safety of new drugs, procedures, or medical devices. There are *3 major phases of clinical trials* that are done in coordination with the US Food and Drug Administration (FDA).

- If it successfully makes it through all 3 phases, it may be submitted for approval for use to the FDA who will approve or reject it based on the data obtained from the clinical trials. If approval is given, monitoring continues indefinitely while the drug is on the market.

- **Phase I**- Consists of drug safety studies in healthy human volunteers. The goals are to make sure the medicine has no major safety issues, and that it reaches the targeted body area and remains there long enough to benefit the patient.
- **Phase II**- Tests whether a drug works in a small number of patients affected by the disease. (Sometimes patients not affected by the disease are used in this stage when appropriate.) The goals are to study the effectiveness of the medicine's ability to treat the disease (or prevent it), and to find the appropriate dosage level.

- **Phase III**- Tests whether the drug works in a large number of patients affected by the disease. The goals are to show the safety and effectiveness of the medicine, to confirm dosage levels, identify side effects, build knowledge of the medicine benefits and risks, and to compare the results against any existing treatments.
- **Post-Marketing Surveillance**- The drug maker and the FDA continue to monitor the drug for side effects while it is on the market. Drugs are taken off the market if previously undetected side effects occur.

- The drug discovery process can take up to 15 years or more to progress from finding a disease target to getting FDA approval. Basic research and preclinical trials can last about 3-6 years. Clinical trials can last about 6-7 years. FDA approval can take anywhere from ½-2 years. Post marketing surveillance is done the entire time the drug is on the market.

DISCOVERING NEW MEDICINES

Human bodies are good at fighting disease, but sometimes things go wrong and then we need medicines.
It takes about 15 years to make a new medicine. This is how it's done.

Basic research

Basic research is sometimes called 'pure' research. Scientists study how bodies and diseases work and search for 'targets' for new treatments. Some basic research involves animals.

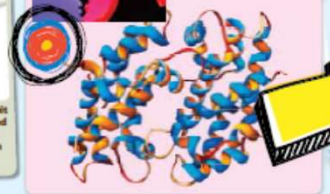
Basic research on fruit flies has helped us find treatments for heart disease and cancer in humans.

FACT In the UK it is illegal to use an animal in research if there is a realistic alternative.

The target

Medicines need 'targets' to act on. A target is something that causes disease, often a protein molecule. It is called a 'target' because we can aim new medicines at it.

If a protein molecule is causing a disease, scientists can look for another molecule that will attach itself and neutralise it. This is sometimes called the 'lock and key' approach.



Finding treatments

When you have a target, you can look for an 'agent' that will act on it.

Many agents have been found in nature, such as digitalin which comes from the common foxglove. But these days we can also make new compounds in the lab or with computer models, and screen them to see if they attach to the target.

Modern technology makes it possible to screen hundreds of thousands of compounds to find a few hundred that work on the target. The ones that work are called 'drug leads'.

FACT Every procedure using an animal in the UK requires three licences from the government.

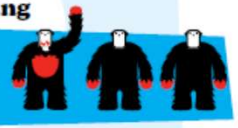
Pre-clinical testing

Screening tells us a lot but chemicals often work differently in living bodies. The most promising new treatments are tested in tissue samples and in some animals to see if they really work. Will they get changed by the digestive system? What are the side effects?

All mammals are more or less the same on the inside. This means that testing on animals can give us a lot of information about how chemicals will work in humans. We can't get this information any other way because nothing else is as complex and unpredictable as a living body.

Safety testing

FACT It is illegal in the UK to use gorillas, chimps, or any other great apes in medical research. Except for human beings, of course.



Only a few compounds make it past the pre-clinical tests. But before we can give them to people, we still need to know how much is safe to take. Nearly everything is poisonous if you take too much. The law requires that compounds are tested for safety on two species of animal.

FACT Eight out of ten animals used in medical research are rats and mice.

Clinical trials phase 1

After a compound has passed safety testing in animals we can begin to test it on people. In the first phase of clinical trials a very small amount of the new treatment is given to a few healthy people to make sure there are no ill effects.

Most phase 1 trials only use men because men can't get pregnant.

Clinical trials phase 2

In phase 2 the treatment is given to a larger group of volunteers who suffer from the target illness.

Clinical trials can be stopped at any stage if there are bad side effects or other problems. Sometimes more animal or tissue tests will have to be done before they can restart. Many Phase 2 trials don't make it to Phase 3.

FACT Each new medicine is tested on 15 times as many people as animals.

Clinical trials phase 3

The third phase of clinical trials uses thousands of patient volunteers in double blind randomised tests.

The 'placebo effect' is what we call it when people feel or even get better just because they think they have taken a medicine. It can be very strong and very strange. A blue placebo works better than a white one, for example, and a placebo injection is much more effective than a placebo pill.

The volunteers don't know if they are getting the active treatment or a placebo (a placebo looks like a real pill but it doesn't have an active ingredient). The people handing out the pills don't know who is getting the placebos either, that is what 'double blind' means.

Approval

If a treatment is more effective than the placebo in the clinical trials it is possible to apply for a licence from the government. A licence means that doctors can give the new medicine to patients.

FACT On average, it costs more than £1 billion to create a new medicine.

Prescription and monitoring

When doctors start prescribing the medicine it is still monitored for side effects and effectiveness. This is sometimes called the 'phase 4 clinical trial'.

You can find out more about how animals are used in discovering new medicines here . . . www.understandinganimalresearch.org.uk

BIOMEDICAL RESEARCH EDUCATION TRUST

Understanding ANIMAL RESEARCH