

## Experimental Medicine: A Platform for Cooperation between Medicine and Veterinary

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### Opening Remarks

Experimental Medicine has a key to open doors to Translational Research. It was said to be originated by Dr. **Claude Bernard** (1813-1878). The book entitled « Introduction to the Research for Experimental Medicine » published in 1865 has been often picked up as a classic in which he had made it clear the necessity and rationale of experiments for modern medicine. I am not totally for the sacrificed animals instead of human but I feel confident that there resides the universal truth how he has positioned the Experimental Medicine.



(Picked up from the Internet)

Dr. Bernard thought «Science is firmly established not only through observation but through experiments». He cast antithesis against notional convention medicine (in his word « Medicine on phylosophical framework ») ; the treatments were given without checking the body construcion nor function in ancient days. It is clear even in the modern medicine that it is extremely difficult to agree to the therapy without scientific proof. Also he insisted that «Medicine should not be based on observation medicine. It should be based on experimental one ». He defined that « **Observation** is to seek for natural phenemenon, on the other hand, **Experiment** is to seek for the phenomenon modified by the researcher ». It is to say that observation is to passively act against given opportunity to study natural phenomenon and experiment is to act proactively toward natural phenomenon and research for artificially modified one. In his thoughts he has not referred shortsightedly that animals except human should be sacrificed. He said «Physicians are making therapeutic experiments on patients every day and surgeons are doing anatomical experiments on patients as well. Therefore, it is translated that we can do experiments on human». However, I need to pay utmost attention to how much degree we can extend experiments and vivisection to human.

Here shows up experimental animal for the first time. He said «I personally agree to the rights (sacrificing experimental animals). In other words, it is irrational to be against

the rights to use experimental animals for researches as one of the most beneficial science for humankind while it is allowed to kill animals as livestock or for daily foods. There exists no reason why we have to hesitate. Life science can be established only through experiments. Dr. Bernard is said have clearly accepted experiments and vivisections with animals. Despite that I have gone through numerous sacrificed animals for the purpose of developing new therapies for patients, I have never come to an idea even once. I have no problem with sacrificing animals. Dr. Claude Bernard's last and definitive comment shows us an inevitable reality. Because he had to take experimental animals into consideration as alternative measures to test artificially-modified new treatment medicine and technology before testing on human body based on his ethics that he was extremely against experiments on human body directly.

### **The responsibilities for and benefits from experimental animals should be shared equally between medicine and veterinary**

As I am a medical doctor, I am always thinking that we need to position experiments with animals in higher priority. One of the reasons is that medical doctors make money through operations to human patients while no money is generated through the operations with rats and pigs. It is a mere fact that more revolutionary skills and techniques are required in most cases to operate with experimental animals using up relatively big funds for research compared to that of the current clinical techniques. However, it is very common that experiments with animals tend to be done by surgeons for the purpose of getting PhD degree before mastering clinical medicine during their spare time, to be frank. What is happening to the veterinary? Those who have desires to become veterinarians do like animals, do they hate to be in a position to deal with experimental animals? It is no way to justify to take away lives of animals whatever reasons you should have. It is no question that the progresses of medicine and veterinary have been greatly owing to experimental animals. The responsibilities stay the same with these two medicines.

### **Face experimental animals with the-state-of-the-art surgical technique**

Regardless human or animals, the most important factor in case of operations is skills and techniques for both medicine and veterinary. The author as a medical doctor has been teaching experimental microsurgery technique using rats & mice and clinically extended this technology for reconstructing hepatic arteries in living-donor liver transplants, anastomosis that is carried out in a severely limited field of view and it resembles brain surgery in difficulties. On the other hand, as a researcher to develop microsurgery, I have been giving a series of trainings to veterinarians who want to provide their veterinary clinical fields with high-end skills and techniques of microsurgery. And after my transfer to Keio University School of Medicine last spring, I have set up a training course on microsurgery for veterinarians (ISEM Japanese East Chapter, Dr. Ishii as a Director). Lots of passionate clinical veterinarians get together at Keio to brush up their microsurgical knowledge and technique (As per the photo below).



(6<sup>th</sup> ISEM Japanese East Chapter training session held on November 26<sup>th</sup>, 2014 at Keio University School of Medicine)

### **New trials with the veterinarian college on experimental medicine**

In 2015 I have set forth a new co-research with Prof. Yoji Hakamata of Nippon Veterinary and Life Science University for generating new rat model applicable for regenerative medicine. Prof. Hakamata was my colleague working together on experimental medicine at Jichi Medical University for 10 years when I had been assigned to the professor & director over there. The objectives were to develop efficient screening models based on experimental medicine and to act as a training material to elevate experimental technique of supportive technicians dealing with animals. And the final goal was to make full use of the developed model for enhancing academia-industry collaboration.

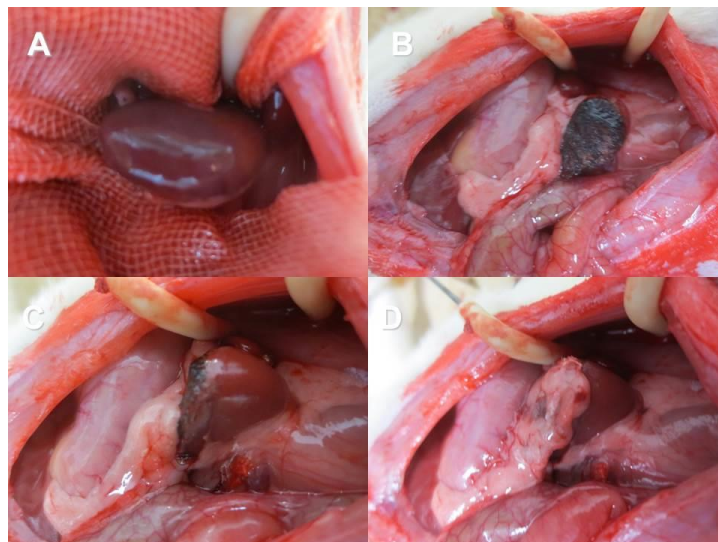
Efficient experimental animal models are indispensable for the development of innovative medical technique and new drugs. The rat is a perfect animal for microsurgical training, because its physiology is well understood, and (unlike mice) rats are large enough for reasonably easy surgical manipulation. When the researchers master these standard microsurgical skills, several models will be provided from the point of clinical settings as the below.

### Rat regenerative medicine evaluation model

Organs	Models	Evaluation type	Reference
Liver	Hepatectomy in excess	Survival Fraction Liver Function	<i>Kawano K, et al. Transplantation 1989</i>
Kidney	5/6 Kidney Removal	Kidney Function BUN,Cre	<i>Cavaqlieri RC, et al. Transplant Proc 2009</i>
Heart	Cardiac Infarction	Pathology	<i>Takahashi M, et al. J Car Vas 2003</i>
Cartilage	Meniscus Damage	IVIS Pathology	<i>Horie, Sekiya, et al. Stem Cells 2003</i>
Brain	Cerebral Infarction	Pathology	<i>Hakamada Y, et al. BBRC 2001</i>
Nerve	Spinal Injury	BBR Score	<i>Endo T, et al. BBRC 2009</i>

(Kobayashi E & Hakamata Y 2014)

In the renal model, 5/6-nephrectomy is usually done without microsurgery. Animals undergo partial left nephrectomy by 2/3 resection of the upper and lower thirds of the left kidney. Following a week, surgical complications were found and a right nephrectomy was finally made in the adequate rats. On the other hand, I recommend a refined method of making 5/6-nephrectomy in rats with micro-surgery.



Under the microscope, after laparotomy we blocked off blood flow to the 2/3 renal region by encircling 2-3 renal arteries with loops of ligatures (A) and then tightening the loops. Taking care of not damaging renal pelvis, congested section was ablated with electrical scalpel along the line between the normal and congested section (B). After ablating the 2/3-left kidney we continuously wrapped up a renal pelvis in a momentum with adhesion bond (C & D). At the same time, the right kidney was removed totally.

**Closing remarks**

The report has been edited based on my thought for those who get involved as start-up members of co-research between Keio University School of Medicine and Nippon Veterinary and Life Science University to remind that experimental medicine is important both from medical and veterinary points of view.

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