What is the "Conscience" of Medical Specialists in Japan?

Abstract:
Medical specialists (scientists, doctors, nurses, pharmacists, etc.) are under strict scrutiny in contemporary society as they are held to a high standard and their crimes are loudly broadcasted through the mass media. In this study, we introduce three cases including the Novartis Case involving a pharmaceutical company employee, the Mazindol Case involving a doctor, and the Muscle Relaxant Case involving a practical nurse. We analyzed each case, studying the risk and protective factors, to determine what caused the above-mentioned medical specialists to commit medical malpractice. In addition to identification and discussion of the key risk factors involved in each case, we propose prevention measures for medical specialists, particularly scientists, in order to avoid similar acts of misconduct in the future. We conclude that additional education and transparency regarding work performance are necessary to prevent such violations. To eliminate
doubt, we recommend that electronic recording devices be used by medical specialists during experimentation.

**Key words:** ethics, risk factor, protective factor, transparency
Introduction

In Japan, there are numerous cases of crimes, such as murder, bribery, and fraud, which are committed by private sector medical professionals, including scientists, doctors, nurses, pharmacists and other medical workers, hereinafter termed medical specialists (MSs).

Why do MSs commit crimes? Why do they commit substantial errors? Some errors are involuntary human errors, simply caused by carelessness. However, some instances of malpractice are intentional. In this study, we focus on egregious misconduct by MSs, particularly crimes associated with research papers or expert opinions, in order to identify causes and to suggest appropriate countermeasures and solutions.

1. Criminal Cases committed by MSs

1) The Novartis Case

Nobuo Shirahashi, Chief Director of Scientific Affairs at Novartis-Pharma, collaborated with several scientists at the Kyoto
Prefectural Medical College to perform data analysis on valsartan, a medication used to treat high blood pressure in current and former patients with conditions such as coronary artery disease (CAD), brain blood vessel disease, and diabetes.

The scientists conducted clinical trials on the efficacy of valsartan, an angiotensin receptor blocker, in reducing further risk among patients with conditions including stroke, angina pectoris, and myocardial infarction. Results of the clinical tests were recorded as the “Kyoto Heart Study” (KHS)\(^1\). The research showed that the group of patients receiving valsartan had a reduced risk of disease compared to patients not receiving the medication.

Based on the KHS, Shirahashi conducted a sub-analysis on the effects of valsartan and utilized the results as an advertisement to sell valsartan under the brand name “Diovan.” He then submitted the data from the sub-analysis to KHS scientists, and they in turn wrote two papers referred to as the calcium channel blocker (CCB) paper and the CAD paper.
Shirahashi divided patients in the CCB paper into two groups: one group was given a CCB medication, and the other group did not receive the medication. These two groups were then divided into two smaller groups, one that received valsartan and one that did not. Results of the analysis showed that the group that received both CCB and valsartan were at lowest risk for disease\(^2\).

For the CAD paper, Shirahashi divided former CAD patients into two groups, one receiving valsartan and the other not receiving valsartan. The results showed that the group receiving valsartan was at lower risk for disease. Therefore, he successfully proved the effectiveness of valsartan to control the specified diseases, and created charts and narrative based on the data\(^3\).

Truthfully, however, the data was altered. In both papers, Shirahashi increased the number of disease events in the group that was not given valsartan. Moreover, on the CCB paper\(^2\), he falsified numbers regarding the statistical value of the events between the valsartan and non-valsartan groups. He submitted
the falsified charts and papers to the KHS scientists who believed the results. Consequently, the scientists submitted false papers regarding the effect of valsartan to various journals\(^4\).

A few years later, the false data in the above papers were revealed by several scientists\(^5\). In January 2014, the Ministry of Health, Labor & Welfare turned the suspect accused of falsifying the data over to the Tokyo District Public Prosecutors Office (TDPPO). In June 2014, the Special Investigation Department of TDPPO arrested Shirahashi and prosecuted him, along with Novartis-Pharma, in the Tokyo District Court. At the trial, both Shirahashi and Novartis-Pharma denied committing a crime.

Finally, in March 2017, the District Court found both parties not guilty, even though the judges recognized that the data were intentionally falsified. The reason for a not guilty finding was purely a legal matter. According to the Pharmaceutical Affairs Law, it is prohibited to advertise, write or circulate false or exaggerated articles with regard to medicines' names, manufacturing measures, effects, and so on. The judges decided that the CCB paper and the
CAD paper were admitted as research papers and not as advertisements for the sale of medicines. Therefore, Shirahashi’s conduct was not a crime. However, this interpretation of the law is clearly wrong because even research papers are included in “articles,” and these are utilized by businesses to increase the sale of medicine.

The TDPPO filed an appeal with the Tokyo High Court and that trial is currently in progress.

2) The Mazindol Case

Mazindol is a medication that affects the central nervous system to reduce appetite. As this medicine can be habit-forming, it may not be prescribed without a medical examination by a licensed doctor. In this case, Singo Kazamoto, a physician, performed initial examinations on patients with obesity. Then, to meet the demands of owning several health clinics across Japan, he ordered nurses to directly supply the mazindol pills (brand name Sanorex), without a prescription, to patients who did not
have any irregular health conditions. Dr. Kazamoto's conduct was a violation of Article 17 of the Medical Practitioner's Act, which states that "no person except a medical practitioner shall engage in medical practice".

The Narcotics Control Department of the Ministry of Health, Labor & Welfare initiated an investigation into Dr. Kazamoto's alleged crime. They found his conduct to be illegal on the basis that the law directs doctors to examine patients directly when prescribing such dangerous medicine.

Public prosecutors of the Osaka District Public Prosecutors Office, arrested Kazamoto and the chief nurse in January 2008. Twenty days later, Kazamoto was indicted. There were some legal problems in this case. The nurses' actions amounted to "medical practice" without the qualifications of a doctor. Therefore, the nurses were punishable. However, Kazamoto did have the qualifications of a doctor. As the conduct of the nurses was estimated to be that of Kazamoto, how do we consider the implications of his qualification as a doctor? Should his conduct be
treated differently than the verdict for the non-qualified nurses? The answer is no, and the reason is that his conduct in ordering the nurses to prescribe without his individual examination of the patients is considered "medical practice" without qualification, because the examination was performed by nurses who did not have any qualifications.

At the trial, defense lawyers insisted that the nurses only assisted the doctor and that their conduct was according to Kazamoto's judgment, and therefore, Article 17 of the Medical Practitioner's Act was not violated.

Finally, Kazamoto was found guilty by both the Osaka District Court and the Osaka High Court because the law in Article 17 states that mazindol is a dangerous narcotic and examination by a doctor is required any time it is prescribed. In particular, the side effects of mazindol, which include thirst, irritability, sleeplessness, and nausea, are serious, and have caused five patient deaths abroad as well as several pulmonary hypertension deaths in Japan. Furthermore, liver failure has been
found in 0.5%~1% of patients and liver cirrhosis is possible with extended use.

3) The Muscle Relaxant Case

This case took place at a hospital in Sendai City in 2000. Daisuke Mori, a male practical nurse, intended to kill patients by administering high doses of Musculax Intravenous (vecuronium bromide), a muscle relaxant, through an intravenous drip. In total, Mori killed one woman and attempted to kill four other people.

He was found guilty and sentenced to life in prison by the Sendai District Court. He later appealed to the High Court and the Supreme Court but his appeals were rejected.

However, in March 2016, he filed an appeal with the Sendai District Court, petitioning for a retrial of his case. According to the Code of Criminal Procedure, a retrial should be granted when there is “new and clear evidence for a finding of not guilty”. Mori’s legal counsel asked a scientist, “Mr. A,” to conduct an experiment on vecuronium analysis, based on new evidence that one of the
victim's blood contained vecuronium.

The process of analysis of the victim's blood at the time of the original investigation was as follows. Two scientists from the Forensic Science Laboratory in a prefectural police headquarters conducted a comparative analysis of standard vecuronium and the blood of a victim. For the purpose of a more accurate analysis, they determined not only molecular weight-related ions, but also precursor ions and fragment ions to substantially increase the ability of the analysis by liquid chromatography-tandem mass spectrometry.

Finally, they found m/z 258 ion in both the standard vecuronium and the victim's blood. One possibility for the occurrence of m/z 258 is that the vecuronium was hydrolyzed, and the substance contained 3-OH vecuronium, creating m/z 258 ion. Therefore, the scientists selected m/z 258 ion as the precursor ion and considered that the blood of the victim contained vecuronium.

Mr. A blamed the two forensic scientists for the results because according to his analysis of vecuronium, only m/z 557 or
m/z 278 ions were found and m/z 258 ions were never found. Accordingly, Mori’s legal counsel submitted the report containing Mr. A’s opinion to the Sendai District Court.

When we criticize the opposite opinion, we must consider the rule that the new experiment must be conducted in an open manner and in the same situation and condition as the previous experiment. However, Mr. A did not conduct his experiment openly, and there was no verification that the two experiments were conducted under identical conditions. This lack of openness and consistency resulted in a rejection of the retrial appeal.

2. Risk factors hindering the “conscience” of MSs

What sort of “conscience” or “integrity” do MSs possess? Sometimes, MSs adhere only to their own opinions and are unwilling to consider opposing views. Is this attitude triggered by honor, status, personality, or monetary benefit? I am afraid the answer is monetary benefit. This element easily corrupts the “conscience” of MSs. In my experience as a public prosecutor for
the Special Investigations Department of the Osaka District Public Prosecutors Office, the temptation of monetary benefit can be enough to encourage misconduct. For instance, the Governor of Wakayama Prefecture received a one million yen bribe for his employment. His motive for accepting the bribe was to collect money for his election campaign foundation. Although he is not an MS, the temptation of monetary benefit can be dangerous to anyone.

We would like to introduce the concepts of risk and protective factors. Risk factors, which may include monetary benefit, self-importance, and the desire to achieve high status and professional success, are circumstances that potentially lead MSs to make corrupt decisions, whereas protective factors like honesty, family stability, and low pressure to achieve success shield individuals from risky behavior.

In this study, we identify the risk and protective factors that exist in the three cases above. In the Novartis Case, the suspect’s motive for falsifying research charts and documents was simply
for monetary gain. Legal regulations are thought to be an effective prevention measure for such behavior.

On April 7, 2017, the Clinical Research Act was enacted (though not yet enforced) in Japan because the Novartis Case caused the Ministry of Health, Labor & Welfare to recognize the necessity of such legal regulations. The features of this law are as follows. Firstly, the main target of regulation is the clinical research conducted by pharmaceutical companies. Under the new law, Specified Clinical Research must be conducted on new medications. In Specified Clinical Research, researchers must submit a practical plan to the Minister of Health, Labor & Welfare after accepting a check by the Designated Clinical Research Judging Committee.

Secondly, during the clinical research, scientists must report to the Minister of Health, Labor & Welfare periodically. They must also keep data, such as the date and place regarding the prescribed medicine.

Thirdly, this law orders pharmaceutical companies to reveal
the amount of funds provided to research scientists every year. The aim of this obligation is to maintain transparent relationships between pharmaceutical companies and researchers.

The above legal regulations are expected to keep pharmaceutical research free of falsification and other corruption. However, punishment would be meted out only when procedures within this specific law have been violated. Therefore, if researchers want to falsify documents or submit counterfeit data related to other studies, it is not punishable under this law. The Designated Clinical Research Judging Committee supervises the conduct of researchers but there is no guarantee that misconduct will be identified. Even when this law is enforced, risk factors are not completely eliminated. How do we confront this problem?

In the Mazindol Case, the same risk factors existed. The doctor understood that his conduct was illegal, but he allowed monetary benefit to take precedence over abiding by the law. How do we confront this problem?

In the Muscle Relaxant Case, the reason that Mr. A concealed
the conditions of the experiment is unknown, but his behavior resulted in the judges' distrust. What caused Mr. A to exhibit such conduct? What were the risk factors in his case? Was it self-importance or monetary benefit? How do we confront this problem?

Our conclusion is that the only solution to the problem is education. The necessity of education to prevent such misconduct has been recognized for a long time; however, ethics education performed thus far has not been enough. I propose that a system of ethics education should be built within society, universities, and colleges. MSs should be provided comprehensive education about risk and protective factors, and how to confront such problems in our society. MS students and interns should also be taught about these factors and problems in universities and colleges. For instance, we propose that a professor in charge of medical ethics education teach them continuously every year, according to their level of understanding.

To be effective, the proposed education initiative should be
led by the Ministry of Health, Labor & Welfare in collaboration with the Ministry of Education, Culture, Sports, Science and Technology.

Because most MSs and medical students do not believe they will ever be faced with such a problem, it is also important to note that ethics education should not be limited to one or two classes. Rather, we must teach them that this issue is a potential concern for all MSs, and can be prevented through systematic medical legal education.

3. How do we save and verify the “conscience” of MSs?

In the Muscle Relaxant Case, Mr. A’s investigation shows the importance of credibility and transparency regarding the experimentation process. How do we save and verify the “conscience” of a MS? I believe we should refer to the rule of investigation interrogation transparency. According to the Code of Criminal Procedure, revised in June 2016, interrogation of severe crimes by public prosecutors and police officers must be recorded
by electronic devices. For reference, severe crimes are provided as follows:

① A crime for which the punishment is the death penalty or life imprisonment.

② A crime in which a victim is killed by intent and its penalties are imprisonment with labor or without labor for at least one year.

③ A case that is investigated by only the public prosecutors, without police officers.

Therefore, we propose the use of an electronic device-recording system at experimental scenes in the field of medicine. We recognize the disadvantages of such a recording system, which include high costs and a complicated procedure, as the same problems exist at law enforcement interrogation scenes. However, these systems are still used in criminal procedures due to the important need for transparency in contemporary society.

There is also a need for transparency of experimental scenes in medical professions. MSs are encouraged to record experiments
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There is also a need for transparency of experimental scenes in medical professions. MSs are encouraged to record experiments
even if they only record the most important components. At the very least, experiments conducted for the purpose of submitting treatments to trial should be recorded by electronic devices, as the processes and procedures of such experiments are often disputed in court. If MSs had recorded their experiments in these situations, many problems would have been alleviated. Moreover, if electronic recording had been performed as a rule among the scientists and experiments related to the stimulus-triggered acquisition of pluripotency cells, the subsequent "STAP Cells Scandal" may have been prevented7-9).

As mentioned above, recording systems are costly; therefore, we propose that the Ministry of Health, Labor & Welfare lead the initiative to distribute recording systems among MSs, as well as subsidize universities and colleges to support the effort. This would allow the Ministry to encourage the recording of experimental scenes in the medical field.

4. Conclusion
Prevention of misconduct and crimes committed by MSs is an urgent matter in our society. The elimination of risk factors and the development of protective factors are needed. Legal regulation is one approach but it is not perfect. Ultimately, the best measure to prevent the misconduct of MSs is through education. Additionally, experimental processes and procedures should be more transparent. For this purpose, an electronic recording system should be implemented, especially to use as evidence at trial. The Ministry of Health, Labor & Welfare would be expected to instigate and enforce such measures to fulfill its governing responsibilities.

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open-label, blinded endpoint morbidity-mortality study. 

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