

# Congenital Anomaly as an Occupational Disease in Korea

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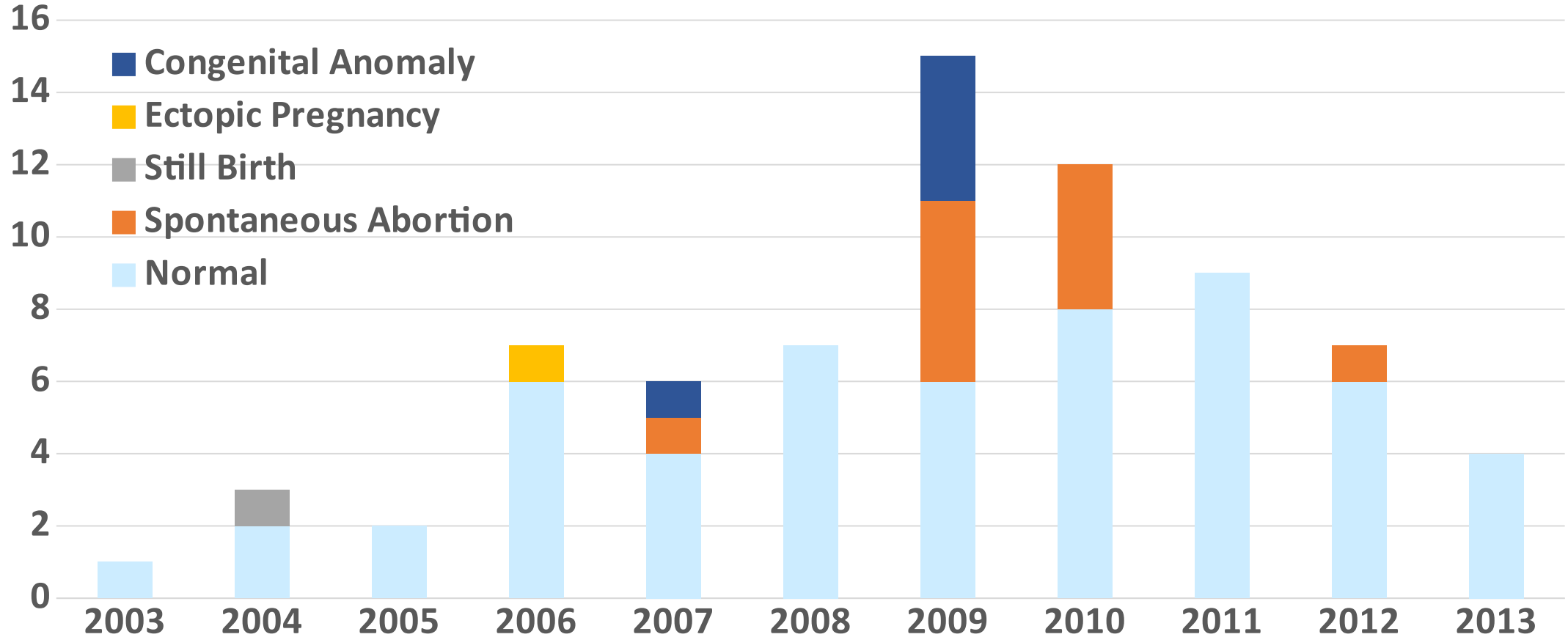
# As it happened

- Clusters of spontaneous abortions and offspring with congenital heart diseases in 2009 and 2010
- 2011, Hospital Workers Labor Union requested an epidemiologic investigation
- 2011~2012, Seoul National University team began the study
- 2014, Korean Workers' Compensation and Welfare Service denied the compensation for offspring's congenital anomaly, while accepting miscarriage as occupational
- 2020, Korean Supreme Court returned the cases of congenital anomalies, in favor of compensation

# Study Site and Population

- Community Central Hospital, Jeju Province, Korea
- 2002, translocated to new buildings with 297 beds in the outskirts of the Jeju city
- At the time of translocation, hospital had recruited new batch of employees, and newly graduated nurses began to work, marry and then get pregnant over time
- Because of the distance from the city center, hospital became a bit like a geriatric nursing hospital for dementia and stroke patients
- 2011, 144 hospital employees, with 65 nurses

# Pregnancy Outcomes by Year



# Congenital Anomaly Incidence, Korea (/10,000)

	Whole Nation		Jeju Province		Study Site	
	2005 년	2006 년	2005 년	2006 년	2002-11 년	2010 년
All Congenital Anomaly	272.9	314.7	197.43	199.79	1111.1	5000
심실중격결손증 (Ventricular septal defect: VSD)	36.09	40.57	40.54	39.61	666.7	3750
폐동맥판막폐쇄 / 협착 (Pulmonary valve atresia and stenosis)	4.85	4.89	3.53	5.17	222.2	1250
동맥관개방 (Patent ductus arteriosus)	12.99	15.82	7.05	1.72	444.4	1250

# Drug Dispense for Inpatients before 2011

- About 60~80% of patients could not swallow pills, and had required the drugs to be powdered
- Nurses at the wards had to powder the pills to dispense the drugs
- Some used electric mixers, and others used mortar jar because it produced less dust
- Hospital had purchased the mixers, and distributed them to the wards
- Pharmacy did not have information on drugs about the FDA pregnancy categories at the time of study

# FDA Pregnancy Categories

- **Category A:** Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
- **Category B:** Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.
- **Category C:** Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- **Category D:** There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- **Category X:** Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

FDA Category D		FDA Category X	
품목명	성분	품목명	성분
자나팜정 **(명인)	alprazolam	달마돔정 **	flurazepam
코다론정 (사노피)	Amiodarone	리피스톱정	atorvastatin
아테놀정	atenolol	리피토정	atorvastatin
로테날정	atenolol	아시트과립 (셀트리온)	acitretin
카마제핀 CR 정	carbamazepine	콜레스논정	simvastatin
리버티정	chlordiazepoxide	프로스카정	finasteride
리보트릴정	clonazepam	졸민정 **(명인)	triazolam
콜킨정	colchicin	와르파린나트륨정	warfarin
삼진디아제팜정	diazepam	왈파정	warfarin
리튬정	lithium carbonate	조코정	simvastatin
아티반정	lorazepam	메바로친정	Pravastatin
메티마졸	methimazole	크레스토정	Rosuvastatin
파록세틴정	paroxetine	<p><b>Category D</b> 태아에 대한 위험이 증명되었으나 산모에 사용함으로써 얻는 이익이 태아에 대한 위험보다 큰 경우 (임부의 생명이 위급한 경우나 다른 약물로 효과가 없는 경우에만 부득이하게 사용)</p> <p><b>Category X</b> 인체와 동물 모두에서 태아의 기형이 증명된 약물 (임산부, 가임 여성에게 금기)</p>	
팍실 CR 정	paroxetine		
세로자트정	paroxetine		
페노바르비탈정	phenobarbital		
페니토인정	phenytoin		
안티로이드	prophylthiouracil		
테라싸이클린캡셀	tetracycline		
토파맥스정	topiramate		
올트릴정 (명인)	valporate		
올트릴정 (보관)	valporate		



# What other factors were investigated?

## **Work**

- X-ray
- Hospital infections: scabies and lindane
- Ergonomics, shiftwork
- Occupational stress: violence, sexual harassment, labor relations, effort-rewards
- Powdering of drug pills

## **Personal**

- Age
- Tenure
- Birth order
- Previous abortion history
- Drinking, smoking
- Previous medical history
- Hobbies

# Analysis

- Case-control approach
  - Almost all nurses did the same tasks
    - Drug powdering task: 100% among case, 80% among controls
  - Not much variation in the exposures
- Before versus After approach
  - Stopped powdering pills at the wards in 2010
  - Waited 1 more year until 2013 for the follow-up
  - Before the stop versus after the stop Analysis
    - Pregnancies with or without powdering tasks

# Overall Results

	2003-2008	2009-2010	2011-2013
	N(%)	N(%)	N(%)
<b>Normal Delivery</b>	<b>23(88.5)</b>	<b>18(66.7)</b>	<b>19(95.0)</b>
<b>Fetal Loss (SA, SB, EP)</b>	<b>3(11.5)</b>	<b>9(33.3)</b>	<b>1(5.0)</b>
<b>Normal baby</b>	<b>22(95.7)</b>	<b>14(77.8)</b>	<b>19(100.0)</b>
<b>Congenital Anomaly</b>	<b>1(4.4)</b>	<b>4(22.2)</b>	<b>0(0.0)</b>
<b>Normal Baby</b>	<b>22(84.6)</b>	<b>14(51.9)</b>	<b>19(95.0)</b>
<b>Fetal Loss + CA</b>	<b>4(15.4)</b>	<b>13(48.2)</b>	<b>1(5.0)</b>

# Before vs After Analysis

	OR(95% CI)	p-value
<b><i>Fetal Loss (SA, SB, EP)</i></b>		
2011-2013	REF	
2003-2008	2.5(0.24-25.81)	0.79
2009-2010	9.5(1.09-82.72)	0.01
<b><i>Fetal Loss + Congenital Anomaly</i></b>		
2011-2013	REF	
2003-2008	3.5(0.36-33.62)	0.8
2009-2010	17.6 (2.06-151.11)	0.001
*Logistic regression, SA: spontaneous Abortion, SB: Still Birth, EP: ectopic pregnancy		

	OR(95% CI)	p-value
<b><i>Fetal Loss (SA, SB, EP)</i></b>		
Powdering task during pregnancy	REF	
No powdering task	3.3(0.72-14.73)	0.12
<b><i>Fetal Loss + Congenital Anomaly</i></b>		
Powdering task during pregnancy	REF	
No powdering task	7.0(1.61-30.45)	0.01
*Logistic regression		

# Work-relatedness of congenital anomaly

- Simultaneous increase in spontaneous abortions as well as congenital anomalies, therefore suggesting overall risks on the range of reproductive spectrums, not just sporadic clusters
- Among work risk factors, significantly associated with drug powdering in both analyses of before and after periods, and also with and without powdering tasks
- No significant difference in other work or personal risks identified

# Congenital Anomaly as Occupational Disease

- Only miscarriage was accepted as occupational by workers' compensation agency
- Congenital anomaly was previously denied by workers' compensation agency
- Based on the argument that affected children are not eligible workers for compensation
- Later acknowledged by Supreme Court
- Based on the argument that the children got the disease at the time of birth and mother and fetus are one body

# Implications

- Congenital anomalies are about 3% of all live births, about 10,000 babies a year in Korea
- How to approach?
  - Outcome Management via Social security? – national health insurance?
  - Source Management via Social regulation, such as workplace reproductive toxins? – how to define and control?
- Industries with high incidence of reproductive problems in Korea
  - Semiconductor industry: working together with SHARP
  - Hospital workers
  - Manual workers