Maternal Abortifacient Use For Clandestine Abortion

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ABSTRACT

Abortion is a highly debated topic. In the United States and other developed countries, the vast majority of abortions performed are done in a clinical setting or under the supervision of clinical staff. However, clandestine abortions still occur. Previously published reports have described clandestine abortions performed using crude and often dangerous methods. In the United States, published reports on the clandestine use of medications for abortions is rare. We report a series of cases in which maternal use of misoprostol and or a combination of misoprostol and mifepristone was used or suspected to have been used for the purpose of at-home pregnancy termination. These medications, purchased from Internet sites, were believed to have been shipped from countries outside of the United States. With ready accessibility to and increased prevalence of these sites on the Internet, it is likely that maternal abortifacient use will become more common in the future. This paper will provide guidance for the investigation and workup of these cases that come to the attention of the medical examiner or coroner. *Acad Forensic Pathol.* 2016 6(4): 663-672

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INTRODUCTION

The medicolegal assessment of fetal and neonatal deaths is often complex and usually requires the assistance of multiple agencies and additional ancillary studies that are not typically requested in adult autopsies. These cases become even more complex when the circumstances surrounding the fetal or infant death are suspicious, unclear, or if viability is in question. Scene investigation may provide critical clues to the proper classification of these deaths.

Case 1

A 20-year-old gravida 2 para 2 (G2P2) woman delivered a male neonate and placenta at home approximately 34 hours after taking tablets that she obtained from an Internet website. She reported that she ordered a “Medical Termination of Pregnancy” kit. According to the website, the kit included one 200 mg tablet of mifepristone and four 200 mg tablets of misoprostol. The mother noted the neonate was larger than she expected and was moving its extremities, so she called for medical assistance. Emergency medical services found the neonate with a pulse and respirations, and therefore cardiopulmonary resuscitation was initiated. The decedent and attached placenta were transported to the emergency department (ED), arriving approximately 50 minutes after delivery. APGARS were unable to be obtained. The neonate had a heart rate of 60 beats per minute with rare respirations. Hospital staff estimated his gestational age to be 18 to 20 weeks. He was deemed nonviable, placed on comfort care measures, and pronounced dead more than one hour after arrival to the hospital (approximately two hours after birth). The mother stated she discovered she was pregnant approximately three months prior and was not receiving prenatal care. She had a history of heavy tobacco use and ethanol and marijuana use during the pregnancy.

At autopsy, the neonate was an atraumatic, normally developed, 410 g white male with body weight, measurements, and organ weights consistent with an estimated gestational age of 20 to 24 weeks. There were no significant gross findings other than slight conges-

tion of the organs. Histologically, there was evidence of terminal hypoxic stress with increased fat deposition in the adrenal fetal cortex and vascular congestion of the organs. The three-vessel umbilical cord had no abnormalities. The placental membranes were thick, slightly opaque, yellow-pink, and were ruptured at a placental margin. The maternal surface of the placenta had no hemorrhages or other irregularities. Microscopically, there was no evidence of chorioamnionitis and the areas of placental membrane thickening noted grossly were consistent with prematurity on histologic examination. The placenta also had areas of villous stromal hemorrhage secondary to placental separation, supporting the presence of a living fetus. Ancillary studies, including bacterial cultures of the lung, blood and spleen, toxicology, metabolic studies, and vitreous electrolyte analysis were all negative or normal. The histologic slides and case information were reviewed in consultation with a pediatric pathologist.

The decedent was delivered at a previable gestational age following self-induction of labor by the mother through the use of abortifacients. Clinical notes report evidence of life upon delivery, but also state that comfort care was initiated due to the decedent’s extreme prematurity. Because the infant was born alive, a death certificate listing a cause and manner of death was necessary. The cause of death in this case was classified as extreme prematurity due to misoprostol-induced labor. The case was certified in this manner because the most likely cause of preterm premature delivery was maternal self-administration of abortifacients; however, a noninfectious placental abnormality such as acute cord compression could not be ruled out with the available clinical information. Due to this uncertainty, the manner of death was classified as undetermined.

Case 2

A 28-year-old G2P2 woman presented to the emergency department complaining of abdominal and back pain and told hospital staff that she was 24 weeks pregnant. Upon examination, it was determined that she was in preterm labor. Her membranes were not ruptured and her cervix was dilated at 1 cm. During

her pelvic examination, the doctor found three hexagonal-shaped pills in her vagina that he believed to be misoprostol. The woman denied placing the pills in her vagina and claimed that she did not know how they got there. Labor progressed, her membranes spontaneously ruptured, and a live male infant was delivered. The mother declined resuscitative measures and the infant died a few minutes after birth. Obtaining the pills taken from the mother's vagina was not possible. The hospital was contacted, but they had already discarded the pills prior to reporting the case.

Autopsy demonstrated a normally developed male neonate. Examination of the placenta, fetal membranes, and umbilical cord revealed no abnormalities; specifically, there was no obvious reason to explain the preterm labor, such as chorioamnionitis. Toxicology testing on postmortem blood was negative. Specific testing of postmortem blood and placental tissue for misoprostol (detection of the biologically active free acid metabolite, misoprostol acid) by liquid chromatography/tandem mass spectrometry did not identify the medication in either of the samples.

The infant was delivered alive, necessitating a death certificate with both a cause and manner of death. Based on the clinical history, it was speculated that the mother self-administered misoprostol resulting in preterm labor with delivery of an extremely premature infant. There were no autopsy or placental findings to offer another etiology for preterm labor. The cause and manner of death were classified as undetermined because maternal abortifacient use could not be confirmed.

Case 3

A 19-year-old G2P0 woman delivered a female fetus at home approximately one day after taking misoprostol tablets that she obtained from the Internet. She delivered the fetus with attached placenta into the toilet, and reported that the baby had no signs of life at the time of birth. Approximately two hours after the delivery, she went to the hospital due to persistent vaginal bleeding. She brought the decedent and the placenta with her and notified hospital staff that she had taken

the pills. Hospital staff estimated the gestational age to be 19 weeks and five days based upon the mother's last menstrual period, and noted that the decedent had no anomalies and was not macerated. The mother had not received prenatal care, and thought that she was eight to ten weeks pregnant.

Autopsy demonstrated a previable, normally developed, 280 g, female fetus with diffuse red skin discoloration. Body weight, measurements, and organ weights were consistent with an estimated gestational age of 19 weeks. There was no visceral congestion. The lungs were submerged in water and did not float. Histologic examination of the organs demonstrated findings associated with prematurity. The lungs had no histologic findings of air exchange. The placenta and umbilical cord were examined, and had no gross or histologic evidence of chorioamnionitis or funisitis, respectively. A focal remote retromembrane hemorrhage was identified on microscopic examination of the placenta, but was not deemed a potential cause of preterm labor. Ancillary studies, including a metabolic screen and bacterial cultures performed on blood, lung, and spleen were noncontributory. Routine toxicology was performed, and was negative. The histologic slides and case information were reviewed in consultation with a pediatric pathologist.

Because there was no evidence of life upon delivery, and the decedent's gestational age was within the age considered to be previable, the cause of death was classified as complete abortion due to misoprostol. No manner of death was used in this case because a fetal death certificate was issued due to the absence of signs of life.

Case 4

A 31-year-old G6P5 woman was transported to the ED with complaints of abdominal pain approximately six hours and 30 minutes after taking 1200 µg of misoprostol that she told hospital staff she purchased from the Internet in order to induce an abortion. She delivered twin boys at an estimated gestational age of 19 to 21 weeks based upon ultrasound examination and the mother's last menstrual period. They had AP-

GAR scores of 2 at one minute and 2 at five minutes. The physicians noted signs of life with evidence of cardiac activity and movement of the extremities, but no respirations. Due to their prematurity, they were placed on comfort care. They were pronounced dead approximately one hour and 30 minutes after delivery.

Earlier in her pregnancy, at a self-reported gestation of approximately ten weeks, the mother reportedly was evaluated in a clinic where she received a prescription for misoprostol for an at home medical abortion. After taking the medication, she had intermittent vaginal bleeding for approximately two weeks and believed she had miscarried. She did not return to the clinic for her follow-up appointment. Two months later, she was evaluated at the hospital after fainting, and was informed that she was still pregnant with twins, and both had fetal heart tones. She did not receive prenatal care, and one month later took the misoprostol that she purchased. The mother had a history of pregnancy induced hypertension and a previous miscarriage.

At autopsy, Twin A was a previable, normally developed 350 g neonate. Twin B was a previable 320 g neonate with a cleft lip and palate, but no other external abnormalities. Both twins had diffusely dense and congested lungs. Body weight, organ weights, measurements, and microscopic examination were consistent with an estimated gestational age of 20 weeks.

Histologically, there was evidence of acute stress response with increased fat deposition in the adrenal fetal cortex and increased apoptosis and macrophages within the thymus. There was also vascular congestion within some organs and predominantly collapsed airspaces within the lungs. The diamniotic, monochorionic twin placenta did not have chorioamnionitis or funisitis; however, it was small for the gestational age (using twin placenta data) and one portion of the placental disc had mildly increased villous maturation with some villi that were appropriate for the gestational age of 20 weeks and others with accelerated maturation. Microbiology cultures and a metabolic screen were noncontributory. Toxicology was negative. The case information and histologic slides were reviewed in consultation with a pediatric pathologist.

The infants were born alive; therefore, a death certificate with a cause and manner of death was issued. Congenital anomalies, infection, and other anatomic and histologic findings associated with perinatal mortality were not identified in either twin. Examination of the placenta did not demonstrate chorioamnionitis; however, it was small for the gestational age. Despite ingestion of a prescribed abortifacient earlier in the pregnancy, the pregnancy continued. The births were later induced by misoprostol that the mother ingested, resulting in preterm labor. In both cases, the cause of death was certified as extreme prematurity. The manner was classified as undetermined because a potential placental abnormality (a small for gestational age placenta) could not be ruled out as a potential contribution to the death.

Case 5

A 25-year-old G2P1 woman with no prenatal care delivered a male fetus at home with no reported signs of life. She presented to an urgent care clinic approximately one day later with complaints of cramping and some vaginal bleeding. She had placed the fetus and placenta in a large purse along with an envelope containing tablets that she had purchased from the Internet, and brought the purse with her to the clinic (**Images 1 and 2**). The mother was transferred to the hospital due to possible retained products of conception. The decedent and placenta were not transported to the hospital with her; therefore, hospital staff could not assess the fetus. The fetus, placenta, and purse were transported to the medical examiner's office. During initial processing, the package containing the tablets was discovered. The tablets were identified as misoprostol (**Image 3**). The mother was interviewed by police. She admitted to taking the pills and stated that she had not felt fetal movement since approximately one week prior to delivery. She reported that when the decedent was delivered, he was delivered feet-first, the umbilical cord was wrapped around his neck, and there were no signs of life. After a thorough police investigation, which included a scene investigation, there were no suspicions that a live birth occurred.

Autopsy demonstrated a normally developed 970 g male fetus with intact skin with prominent red to purple-red skin discoloration of the buttocks and lower extremities. Body weight, measurements, organ weights, and histologic findings were consistent with an estimated gestational age of 27 to 28 weeks. The lungs were submerged in water and did not float. Microscopic examination was significant for findings associated with acute stress response and there was no evidence of air exchange within the lungs. Gross and microscopic examination of the placenta demonstrated a small for estimated gestational age placenta without chorioamnionitis or funisitis. Microbiology cultures and a metabolic screen were noncontributory. Routine toxicology was negative.

Because the decedent was stillborn, a fetal death certificate was issued, and no manner of death was issued.

Image 1: Mother's purse in the urgent care clinic.

Image 2: Decedent found wrapped in a T-shirt inside of a purse.

The cause of death was classified as third trimester fetal demise due to induced labor with misoprostol.

DISCUSSION

Misoprostol and Mifepristone: Pharmacology, Pharmacokinetics, and Detection

Misoprostol is approved by the U.S. Food and Drug Administration (FDA) for the use of reducing the risk of the development of gastric ulcers associated with nonsteroidal anti-inflammatory medications (NSAIDs). It is marketed as an oral preparation and was first approved in the United States by the FDA for use in 1988. In 2012, pregnancy was designated as a contraindication to the use of misoprostol for prevention of NSAID-associated gastric ulcers in this patient population (1). Misoprostol is a synthetic prostaglandin E1 analog that has effects on the gastrointestinal tract by decreasing gastric acid secretion and increasing bicarbonate and mucous production in the stomach. It causes uterine contractions, and for obstetrics and gynecological purposes, is administered in oral, buccal, sublingual, vaginal, and rectal preparations. There are various dosage recommendations for each

method of administration (1, 2). Misoprostol is rapidly metabolized to the active metabolite, misoprostol acid, and has a very short half-life of 20 to 40 minutes. Because of its rapid metabolism, misoprostol and its metabolites may be difficult to detect; however, there are published reports of detection of the active metabolite misoprostol acid in plasma, serum, urine, and breast milk by gas chromatography-mass spectrometry (GC/MS) and combining liquid chromatography-mass spectrometry (LC/MS) methods with GC/MS (1-5). Mifepristone, also known as RU-486, is a progestin antagonist that is approved in combination with misoprostol for terminating pregnancies up to 70 days estimated gestational age. When used in combination with misoprostol, the typical regimen is a single dose (200 mg) of mifepristone taken orally, and then one to two days later, four doses of misoprostol (800 µg total) are taken simultaneously, placed along the buccal mucosa or within the vagina (2, 6). Mifepristone acts on the pregnant uterus by causing decidual necrosis, uterine contractions, and cervical ripening, resulting in expulsion of the products of conception (6).

Misoprostol is used off-label in obstetrics and gynecology practice for medical abortions, cervical ripening for preparation for surgical procedures (surgical abortion, hysteroscopy), induction of labor, management of miscarriages, and management of postpartum hemorrhage (2, 7). This off-label use of misoprostol is only to be used in a clinical setting (1). An Internet search yields many websites that offer instructions on how to abort a pregnancy using the combination of misoprostol and mifepristone or misoprostol alone. The websites also sell these medications or refer women to websites where they can purchase them. The author(s) of the site may or may not provide information about the potential complications associated with these medications and are providing medical advice on dosage amounts based upon recommendations obtained from medical sources such as the World Health Organization (WHO), which has issued policy recommendations pertaining to surgical and medical abortions (8). The author(s) of these sites also reference various nonmedical sources and interpretations of journal articles.

Image 3: One of three packets recovered from an envelope in the mother's purse.

Mifepristone has been associated with sepsis and persistent uterine bleeding requiring transfusion or surgical intervention, but this is rare (2, 6). Potential complications associated with misoprostol use include congenital anomalies as a consequence of a continued pregnancy after failed abortion, uterine rupture, and more benign side effects such as nausea, vomiting, and diarrhea (2). Fetal demise due to misoprostol is not because of the direct toxicity of the medication to the fetus, but due to its effect on the uterus (i.e., uteroplacental blood flow, contractions) resulting in essentially an unstable environment for the fetus and subsequent pregnancy loss.

Clinical and Legal Terminology

Various terminology exists relating to fetal and infant deaths and it is important to have a good understanding of these terms. Select terms are discussed, and reiterated in **Table 1**. The National Center for Health Statistics of the Centers for Disease Control and Prevention defines live birth as the delivery or extraction of a product of human conception, irrespective of the duration of the pregnancy, which, after delivery or extraction, breathes or shows any other evidence of life, such as a heartbeat, umbilical cord pulsation, or definite movement of voluntary muscles, regardless of whether the umbilical cord has been cut or if the placenta is attached. It also states that heartbeats should be differentiated from transient cardiac contractions, and that breathing should be distinguished from brief respiratory efforts. Fetal deaths are defined as deaths

that occur prior to delivery or extraction and that are not due to an induced termination of the pregnancy. There are no signs of life upon delivery or extraction in these cases (9, 10). A miscarriage, or spontaneous abortion, is defined as fetal demise that occurs in utero prior to 20 weeks gestation. Spontaneous abortion can further be subdivided into multiple categories including incomplete abortion, complete abortion, and threatened abortion (11). Stillbirth describes fetal deaths that occur at or greater than 20 weeks gestation (9, 10).

The medical definition of viability is based on multiple clinical factors. The limit of viability is defined as the stage of fetal maturity in which there is a reasonable chance of survival. A combination of clinical factors including, but not limited to the gestational age at delivery, birth weight, and gender are used to determine viability and the prognosis of extremely premature infants (12, 13). This is used to assist clinicians, in conjunction with the parent(s), in the management of extremely premature infants, who, due to their prematurity, are at increased risk for complications including infections, neurodevelopmental impairment, and death (12, 13). In these complex cases, clinicians are tasked with determining viability; both clinicians and families are faced with the decision to determine what, if any, medical intervention is appropriate. The National Institute of Child Health and Human Development Neonatal Research Network studied more than 4000 extremely premature infants who were delivered at 22 to 25 weeks gestational age. Their aim

Table 1: Common Terminology Relating to Fetal and Neonatal Birth and Death

Term	Definition
Live birth	Delivery or extraction of a product of human conception, which, after delivery or extraction, shows evidence of life
Fetal death	Death that occurs prior to delivery or extraction and that is not due to an induced termination of the pregnancy; no evidence of life upon delivery or extraction
Miscarriage (spontaneous abortion)	Fetal death that occurs in utero prior to 20 weeks gestation; can be subdivided into categories including threatened abortion, complete abortion, and incomplete abortion
Stillbirth	Fetal death that occurs at or greater than 20 weeks gestation
Limit of viability	Stage of fetal maturity that ensures a reasonable chance of extrauterine survival
Term	Birth occurring at or greater than 37 weeks
Extreme prematurity	Birth that occurs before 28 weeks gestation

was to determine if additional clinical factors besides gestational age, such as gender and number of births, could aid in the estimation of prognosis. They found that singleton births, female infants, infants who were exposed to antenatal corticosteroids, and infants born at 25 weeks gestation had a significantly decreased risk of death and/or neurodevelopmental impairment (13). Of the infants within the gestational ages selected in the study, infants born at 22 weeks gestation had the highest risk of mortality and morbidity (13). The American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine, and several other organizations do not recommend neonatal resuscitation at less than 22 weeks gestation (12).

A term pregnancy is defined by ACOG as a delivery that occurs at or greater than 37 weeks gestation and can be further subdivided into early term, full term, and late term (14). The American College of Obstetricians and Gynecologists further defines extreme prematurity as births that occur before 28 weeks gestation. In the United States, the legal definition of viability and the regulation of abortions is determined by the laws passed by individual states and territories, and many defer to the treating physician in the determination of viability (15, 16).

Legality of Maternal Abortifacient Use

These controversial cases raise several legal and ethical questions. Is it legal to purchase these medications online without a prescription from a treating healthcare provider? Does the mother have the legal right to abort a pregnancy without being under the supervision of a healthcare provider? If it is determined that she purchased and used these medications with the intent to abort the pregnancy, can and will she be prosecuted?

The Federal Food and Drugs Act of 1906, also known as the Pure Food and Drugs Act, prohibited the manufacturing, sale, and interstate distribution of adulterated or misbranded foods, drugs, and drinks in the United States; however, the law was challenging to enforce (17, 18). The Federal government was required to prove that labeling was false and misleading before a product

could be taken off the market, and also had to prove that the manufacturer of the product intended to mislead and defraud customers (17, 18). The organization responsible for evaluating the products was the Bureau of Chemistry within the Department of Agriculture. The Bureau of Chemistry later became the U.S. Food and Drug Administration (FDA) (17, 18). The Federal Food and Drugs Act was repealed and replaced with the 1938 Food, Drug, and Cosmetic (FD&C) Act. This law was passed to create policies that would provide greater protection for consumers against misbranded products (18, 19). An example of a misbranded drug would be a product with a package label stating a proprietary name when in fact the drug was not manufactured by the proprietary company. In 2013, the FDA worked with several international agencies, using the FD&C Act, to combat illegal online pharmacies that claimed to sell brand name and generic FDA-approved medications used to treat diabetes mellitus, erectile dysfunction, and schizophrenia. The websites and millions of dollars worth of medications were seized, and the FDA issued warning letters to the owners of the websites (20). In 2015, the U.S. Attorney's Office indicted an American pharmacist who allegedly owned and operated an online pharmacy in which he filled and shipped prescriptions to clients who did not have a valid physician-patient relationship. These clients filled out online questionnaires, and then an American physician in another state who allegedly worked with the pharmacist authorized the prescriptions to be filled without seeing or examining the buyers (21). According to the indictment, these prescriptions were illegal because a valid physician-patient relationship did not exist (21). Several organizations including the Drug Enforcement Agency (DEA) and the Federal Bureau of Investigation (FBI) were involved in the investigation.

A search for instances of prosecution of women in the U.S. for the purchase and use of illegally procured abortifacients results in rare cases. One woman in Indiana was imprisoned after being convicted of child neglect and feticide after she allegedly ingested abortion pills that she obtained online in order to terminate her pregnancy. A receipt from a pharmacy in China and text messages she sent to a friend were among

the evidence used against her (22). Individual states have varying definitions of viability and stipulations on abortions. Some states also include laws relating to feticide. It is the challenge of the prosecutor within a given jurisdiction to determine how and which laws should be enforced. Due to the variability in these laws, the forensic pathologist should refer to his or her individual state or country's laws if questions should arise.

Determination of Cause of Death and Classification of Manner of Death

The determination of cause and manner of death may be particularly challenging in infant and pediatric cases, and is even more challenging in cases similar to those presented. Thorough evaluation and sampling of all organs and additional tissues, including placenta, is paramount. The placental examination should include appropriate written and photographic documentation that may aid a consultant who is more familiar with these specimens in the identification of subtle gross abnormalities. At minimum, sections of the placenta should include one section of the membrane roll, two sections of the umbilical cord, two full-thickness sections of normal appearing placenta away from the placental margin, and sections of gross abnormalities. The purpose is to identify the presence, if any, of infant or placental abnormalities that would result in preterm labor. References providing guidance in the examination and identification of gross and microscopic placental abnormalities may be useful in identifying both common and less recognized pathology (22). In cases where maternal abortifacient use is suspected and neonatal and placental etiologies of preterm labor are ruled out through autopsy examination, microscopic examination, and ancillary studies, the medical examiner or coroner is further tasked with proving that one or more of these medications was used. This may be difficult without initial investigative information obtained by hospital personnel and police officers who can assist in identifying the medication or obtaining initial statements from the mother. Although difficult to detect due to its short half-life, misoprostol may be detected in postmortem samples, which would provide additional evidence that it was taken.

In cases of premature live births in which maternal abortifacient use is confirmed, and preterm labor occurred as a result of self-administration of the abortifacient for the sole intent of terminating the pregnancy, a reasonable argument could be made to certify the cause of death as extreme prematurity and the manner of death as homicide. In jurisdictions in which a manner of death is required for fetal death certificates, and the same scenario is present, a similar argument would apply. At the other end of the spectrum for cases where no definitive determination can be made, classifying both the cause and manner of death as undetermined would be appropriate. Understandably, there is a large gray area, and individual case information must be taken into account.

CONCLUSION

The ease of obtaining pharmaceuticals online increases the possibility that medical examiner and coroner's offices will encounter deaths associated with the use or misuse of these medications. Abortifacient medications can be obtained without a prescription from pharmacies outside of the United States. Women who utilize this method of abortion will most likely deliver the fetus at home and may not seek medical care or inform anyone that they gave birth. Unattended births have an increased risk of complications for both the mother and the infant, with the potential for perinatal fetal/infant death. The investigation of these deaths is critical to correctly classify these cases and often relies on multiple agencies. Information from the mother and first responders is needed to help determine live birth versus stillbirth. Late second trimester gestational age fetuses, even though previable, may show signs of life after birth; therefore, a manner of death will need to be classified. It is important that responding law enforcement officers, medical personnel, and medicolegal death investigators inquire about the potential use of abortion inducing medications. Key information such as the type and dosage of medication taken, the route of administration, and the timeframe in which the medication was taken should be obtained. An autopsy and placental examination should be performed on fetuses/infants born at home in order to document anatomic, histologic, or toxicologic find-

ings that could have precipitated the delivery, as well as assess gestational age and viability. Due to its short half-life, identification of misoprostol in postmortem samples is difficult. Finding the tablets on scene may be the only clue that a clandestine abortion has occurred. The legal ramifications of these deaths would depend on the determination of live or stillbirth, the viability of the fetus, and the local/state laws regarding abortion. The forensic pathologist will encounter numerous clinical and legal terms during the investigation of these deaths. The laws vary from state to state and between countries. The medical examiner or coroner should familiarize him or herself with the laws of their region.

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