Alert report for the prevention of recurrence of medical accidents Number 2

Deaths due to Anaphylaxis following Intravascular Administration of Drugs

Since the publication of Recommendation Number 3 “Analysis of deaths related to ‘Anaphylaxis caused by injections’” in 2018, there have been reports of 19 adult cases presenting fatal anaphylactic shock following intravascular administration of drugs, such as contrast media, antibiotics, and antineoplastic agents.
The cause of death in all these cases was anaphylactic shock, including suspected cases.

Note) • In the summary below, all durations mentioned after the initial symptom are measured “from the time of onset of the initial symptom.”
• Drugs are identified by their pharmacological classifications and product names (trade names), and the registered trademark symbol is omitted.

	Illustrative Cases
Case 1	• A patient in his/her 60s with rectal tumor. Ai: present. Autopsy: absent. • The causative drug was an iodinated contrast medium (Iomeron). Anaphylaxis occurred in the CT examination room. • A contrast medium had been used for the patient in the past, but no allergic symptoms had appeared. • A cough appeared immediately after infusion of the contrast medium. One minute after the onset of the initial symptom (during scanning), the patient felt unwell. Two minutes later (at the end of scanning), the patient exhibited pronounced conjunctival hyperemia, cold sweat, nausea, and facial redness, and the physician and other staff were called. Five minutes later, the patient vomited and the consciousness level declined. Adrenaline 0.3 mg was intramuscularly injected, and an emergency call was made. Eight minutes later, blood pressure became unmeasurable and resuscitation was performed, but the patient died about 1 hour later.
Case 2	• A patient in his/her 70s with acute cholangitis. Ai: absent. Autopsy: absent. • The causative drug was a β-lactam antibiotic (Wystal). Anaphylaxis occurred in the hospital room. • A β-lactam antibiotic (Tazopipe) had been used for the patient in the past, and allergic symptoms had appeared. • One to two minutes after the start of infusion of the antibiotic, facial flush, redness of both upper extremities, pruritus, and difficulty in breathing occurred. Drug administration was discontinued and the physician was called. Three to four minutes after the initial symptoms, the patient went into cardiac arrest, prompting the initiation of cardiopulmonary resuscitation and intramuscular injection of adrenaline 0.5 mg. Thirteen to fourteen minutes later, the second intramuscular injection of adrenaline 0.5 mg was given. An emergency call was made 17 to 18 minutes later, and resuscitation was performed, but the patient died the next day.

[Abbreviations] Ai = Autopsy imaging (post-mortem imaging); SpO_2 = percutaneous arterial oxygen saturation; JCS = Japan Coma Scale (classification of consciousness disturbance)

	Illustrative Cases
Case 3	• A patient in his 50s with prostate cancer. Ai: absent. Autopsy: present. • The causative drug was an iodinated contrast medium (Iomeron). Anaphylaxis occurred in the CT examination room. • A contrast medium had been used for the patient in the past, but there was no documentation of allergic symptoms. • One minute after infusion of the contrast medium, pruritus of the upper extremities and nausea appeared. One minute after the initial symptoms, the patient complained of distress and became restless, and an emergency call was made. Four minutes later, the patient lost consciousness. Adrenaline 0.3 mg was administered by intramuscular injection. Seven minutes later, cardiac arrest occurred, and emergency treatment was provided, but the patient died about five hours later.
Case 4	• A patient in his/her 70s with hepatocellular carcinoma. Ai: absent. Autopsy: absent. • The causative drug was an iodinated contrast medium (Iomeron). Anaphylaxis occurred in the CT examination room. • An iodinated contrast medium (Omnipaque) had been used for the patient in the past, and mild allergic symptoms had appeared. • Eight minutes after infusion of the contrast medium, a cough and facial flush appeared. Immediately after the initial symptoms, the consciousness level was JCS III-200 to 300, and an emergency call was made. One minute later, the patient went into respiratory arrest with a carotid pulse not palpable, and cardiopulmonary resuscitation was initiated. Three minutes later, adrenaline 1 mg was administered by intravenous injection. Emergency treatment was provided, but the patient died approximately one month later.
Case 5	• A patient in his/her 40s scheduled to undergo percutaneous catheter ablation for atrial fibrillation. Ai: present. Autopsy: absent. • The causative drug was an iodinated contrast medium (Iopamiron). Anaphylaxis occurred in the CT examination room. • A contrast medium had been used for the patient in the past, but no allergic symptoms had appeared. • Four minutes after infusion of the contrast medium, the patient developed nausea. Immediately after the initial symptom, the patient brought up saliva-like vomit and became restless, and the physician was called. Pallor on the face and cold sweat were also observed. Two minutes later, an emergency call was made. Three minutes later, the patient's blood pressure became unmeasurable, prompting the initiation of cardiopulmonary resuscitation. Four minutes later, adrenaline 0.5 mg was administered by intramuscular injection. Despite emergency treatment, the patient died the next day.

[Abbreviations] Ai = Autopsy imaging (post-mortem imaging); SpO_2 = percutaneous arterial oxygen saturation; JCS = Japan Coma Scale (classification of consciousness disturbance)

	Illustrative Cases
Case 6	• A patient in his/her 50s who had undergone a coronary artery bypass. Ai: absent. Autopsy: absent. • The causative drug was an iodinated contrast medium (Iopamidol). Anaphylaxis occurred in the CT examination room. • An iodinated contrast medium had been used for the patient in the past, and allergic symptoms had appeared. • One minute after infusion of the contrast medium, a cough appeared and the examination was interrupted. Immediately after the initial symptom, the patient developed pruritus of both upper extremities during preparation of the drug. The patient also experienced nausea, and four minutes later, an antihistamine and an H_2 receptor antagonist were administered by intravenous injection. The patient's blood pressure became unmeasurable, and five minutes later, adrenaline 0.5 mg was administered by intravenous injection. Seven minutes later, cardiopulmonary resuscitation was initiated and the patient became temporarily compliant; however, 18 minutes later, blood pressure decreased again, prompting intramuscular injection of adrenaline 0.3 mg. Despite emergency treatments, the patient died approximately six hours later.
Case 7	• A patient in his/her 70s with internal carotid artery stenosis. Ai: present. Autopsy: absent. • The causative drug was an iodinated contrast medium (Iopaque). Anaphylaxis occurred in the CT examination room. • An iodinated contrast medium (Hexabrix) had been used for the patient in the past, and allergic symptoms had appeared. • Two minutes after infusion of the contrast medium (immediately after completion of scanning), the patient developed sneezing and pruritus, and an examination was performed. Two minutes after the initial symptoms, the patient's blood pressure decreased and the SpO_2 was 80%–89%, prompting an emergency call. Four minutes later, adrenaline 1 mg was administered by intravenous injection. The blood pressure became unmeasurable, and cardiopulmonary resuscitation was initiated. Emergency treatment was provided, but the patient died the next day.
Case 8	• A patient in his/her 50s receiving maintenance dialysis with shunt occlusion. Ai: absent. Autopsy: absent. • The causative drug was an iodinated contrast medium (Iopromide). Anaphylaxis occurred in the CT examination room. • An iodinated contrast medium (Iomeron) had been used for the patient in the past, and allergic symptoms had appeared. • After infusion of the contrast medium, the patient developed discomfort in the pharyngeal region during scanning. One to three minutes after the initial symptom (at the end of scanning), the patient developed pruritus and difficulty in breathing, and an examination was performed. The blood pressure decreased, and the SpO_2 became unmeasurable. Two to five minutes later, cold sweat was observed, and adrenaline 0.5 mg was administered by intramuscular injection. An emergency call was made. The patient lost consciousness five to eight minutes later. Emergency treatment was provided, but the patient died about six hours later.

[Abbreviations] Ai = Autopsy imaging (post-mortem imaging); SpO_2 = percutaneous arterial oxygen saturation; JCS = Japan Coma Scale (classification of consciousness disturbance)

	Illustrative Cases
Case 9	• A patient in his/her 70s with suspected acute osteomyelitis of the mandible. Ai: absent. Autopsy: present. • The causative drug was an iodinated contrast medium (Optiray). Anaphylaxis occurred in the CT examination room. • The patient's history of drug allergy was unknown. • One minute after infusion of the contrast medium, the patient complained of discomfort. The drug administration was discontinued, but the patient said that he/she was "in distress," and grimaced. Then, flushing of the upper body appeared. One minute after the initial symptom, the patient's blood pressure became unmeasurable. Three minutes later, an emergency call was made. Redness of the face and both upper extremities was noted, and five minutes later, the patient did not respond when called by name, so adrenaline 0.5 mg was administered by intramuscular injection. Ten minutes later, the second dose of adrenaline 0.5 mg was administered by intramuscular injection. Fourteen minutes later, cardiac arrest occurred and emergency treatment was performed, but the patient died the next day.
Case 10	• A patient in his 70s with prostate cancer. Ai: present. Autopsy: absent. • The causative drug was an MRI contrast medium (ProHance). Anaphylaxis occurred in the MRI examination room. • An iodinated contrast medium (Omnipaque) had been used for the patient in the past, and no allergic symptoms had appeared. • Thirty seconds after infusion of the contrast medium, the patient seemed to be in distress, so the scan was discontinued and the physician and other staff were called. Two and a half minutes after the initial symptom, feeling unwell, generalized redness, and rigidity of limbs occurred. Three and a half minutes later, adrenaline 0.3 mg was administered by intramuscular injection. Seven to eight minutes later, the patient went into cardiac arrest, and emergency treatment was performed, but the patient died about four hours later.
Case 11	• A patient in his/her 80s with pharyngeal pain. Ai: absent. Autopsy: absent. • The causative drug was a β-lactam antibiotic (Ceftriaxone). Anaphylaxis occurred in the clinic. • The patient's history of drug allergy was unknown. • Immediately after intravenous injection of the antibiotic, the needle was removed because the patient was sneezing and complained of "irritability." Immediately after the initial symptoms, facial flush and decreased level of consciousness were observed. Two minutes later, an emergency call was made. The patient's blood pressure became unmeasurable and respiratory arrest occurred, prompting the initiation of cardiopulmonary resuscitation. Thirteen minutes later, adrenaline 1 mg was administered by intravenous injection, and the patient was transferred by ambulance. Despite emergency treatment, the patient died about three weeks later.

[Abbreviations] Ai = Autopsy imaging (post-mortem imaging); SpO_2 = percutaneous arterial oxygen saturation; JCS = Japan Coma Scale (classification of consciousness disturbance)

	Illustrative Cases
Case 12	• A patient in his/her 70s with suspected pneumonia. Ai: absent. Autopsy: absent. • The causative drug was a β-lactam antibiotic (Ceftriaxone). Anaphylaxis occurred in the hospital room. • No allergic symptoms had occurred after use of drugs in the past. • One minute after initiation of the antibiotic infusion, the patient felt unwell and had nausea. Then the drug administration was discontinued. Immediately after the initial symptoms, facial flush and decreased blood pressure were observed, and an emergency call was made. The patient developed cyanosis and wheezing, and the consciousness level was JCS III-300. The patient's pulse became unpalpable, and cardiopulmonary resuscitation was initiated. Ten minutes later, adrenaline 1 mg was administered by intramuscular injection. Thirteen minutes later, the second dose of adrenaline 1 mg was administered by intramuscular injection. Despite emergency treatment, the patient died about three hours later.
Case 13	• A patient in his/her 80s undergoing dental treatment for odontogenic cellulitis of the mandible. Ai: absent. Autopsy: present. • The causative drug was a β-lactam antibiotic (Ceftriaxone). Anaphylaxis occurred in the clinic. • No allergic symptoms had occurred after use of drugs in the past. • Five minutes after initiation of the antibiotic infusion, the patient complained of "distress." The drug administration was discontinued and the physician was called. Immediately after the initial symptom, cyanosis and wheezing developed, and the patient's SpO_2 was 60%–69%. During preparation of medicines, the patient's carotid pulse became nonpalpable, prompting the initiation of cardiopulmonary resuscitation. As the infusion needle had been dislodged spontaneously, 1 mg of adrenaline was administered by intramuscular injection, and an emergency call was made. Four minutes later, cardiac arrest occurred, and the second dose of adrenaline 1 mg was given by intramuscular injection. Thirteen minutes later, the patient was transported by ambulance and emergency treatment was performed. However, the patient died the next day.
Case 14	• A patient in his/her 90s with a urinary tract infection. Ai: present. Autopsy: present. • The causative drug was a β-lactam antibiotic (Ceftriaxone). Anaphylaxis occurred in the hospital room. • A β-lactam antibiotic (Ceftriaxone) had been used for the patient in the past, and mild allergic symptoms had appeared. • Six minutes after initiation of the antibiotic infusion, the patient groaned and lost consciousness. The patient's blood pressure became unmeasurable, and the physician was called. Ten minutes after the initial symptom, respiratory arrest occurred, and airway management was performed. Fourteen minutes later, adrenaline 0.5 mg was administered by intravenous injection. Despite emergency treatment, the patient died about two hours later.

[Abbreviations] Ai = Autopsy imaging (post-mortem imaging); SpO_2 = percutaneous arterial oxygen saturation; JCS = Japan Coma Scale (classification of consciousness disturbance)

	Illustrative Cases
Case 15	• A patient in his/her 70s with hepatocellular carcinoma. Ai: present. Autopsy: present. • The causative drug was a β-lactam antibiotic (Wystal). Anaphylaxis occurred during transfer to the treatment room. • A β-lactam antibiotic (Wystal) had been used for the patient in the past, and no allergic symptoms had appeared. • During the transfer to the treatment room after initiation of the antibiotic infusion, the patient felt discomfort around the face. Four minutes after the initial symptom, it was reported to the physician. Then the patient developed finger discomfort and facial flush. Eight to nine minutes later, ST-segment elevation was noted in the ECG monitor, with unmeasurable SpO_2 and a consciousness level of JCS III. The drug administration was discontinued, and adrenaline 0.1 mg was administered by intravenous injection. A corticosteroid and 0.2 mg of adrenaline were administered by intravenous injection. Thirteen minutes later, the carotid pulse became nonpalpable, so emergency treatment was provided, but the patient died about three hours later.
Case 16	• A patient in his/her 60s with patella fracture. Ai: present. Autopsy: absent. • The causative drug was a new quinolone (ciprofloxacin). Anaphylaxis occurred in the hospital room. • A β-lactam antibiotic (Flomox) had been used for the patient in the past, and allergic symptoms had appeared. • Five minutes after initiation of the antibiotic infusion, poor complexion, shallow breathing, and pupil dilation were observed. The physician was called, and the drug administration was discontinued. Five minutes after the initial symptoms, the patient went into respiratory arrest, prompting cardiopulmonary resuscitation. Ten minutes later, adrenaline 1 mg was administered by intravenous injection. Emergency treatment was provided, but the patient died three days later.
Case 17	• A patient in his/her 70s with peritoneal carcinoma. Ai: absent. Autopsy: absent. • The causative drug was an antineoplastic agent (paclitaxel). Anaphylaxis occurred in the outpatient department. • No allergic symptoms had occurred after the initial use of the antineoplastic agent (paclitaxel). • Five minutes after the start of infusion of the antineoplastic agent (the second dose), the patient developed pruritus on the neck, so the infusion was discontinued. Immediately after the initial symptom, the patient had difficulty breathing. One minute later, the patient's SpO_2 was 80%–89%, and the physician was called. Two minutes later, the patient's respiratory status worsened, so an emergency call was made. Three minutes later, an antihistamine was administered by intramuscular injection. Eight minutes later, the patient went into cardiac arrest, prompting the initiation of cardiopulmonary resuscitation and intramuscular administration of adrenaline 0.3 mg. Thirteen minutes later, the second dose of adrenaline 0.3 mg was administered by intramuscular injection. Despite emergency treatment, the patient died two days later.

[Abbreviations] Ai = Autopsy imaging (post-mortem imaging); SpO_2 = percutaneous arterial oxygen saturation; JCS = Japan Coma Scale (classification of consciousness disturbance)

	Illustrative Cases
Case 18	• A patient in his/her 40s who had undergone a living donor liver transplantation. Ai: present. Autopsy: present. • The causative drug was a plasma derivative (Venoglobulin IH). Anaphylaxis occurred in the hospital room. • No allergic symptoms had occurred after use of drugs in the past. • Immediately after initiation of the infusion of the plasma derivative, the patient defecated in the toilet, and malaise and chest tightness occurred when the patient returned to bed 10 minutes later. Fifteen minutes after the initial symptoms, the patient's SpO_2 was 80%–89%, prompting the initiation of oxygen administration and discontinuation of drug administration. About 30 minutes later, the patient's SpO_2 increased, which led to the resumption of drug administration. About one hour later, the SpO_2 was 70%–79%, and an emergency call was made. About 1.5 hours later, the patient went into cardiac arrest, and adrenaline 1 mg was administered by intravenous injection. Despite emergency treatment, the patient died about five hours later.
Case 19	• A patient in his/her 70s with a rib fracture, who was on chronic maintenance dialysis. Ai: present. Autopsy: present. • The causative drug was a protease inhibitor (Naotamin). Anaphylaxis occurred in the dialysis room. • A protease inhibitor (Nafamostat) had been used for the patient in the past, and no allergic symptoms had appeared. • Because of the bone fracture, the anticoagulant was switched to a protease inhibitor, and dialysis was initiated. Two to three minutes later, the patient reported a sensation of "distress" accompanied by increased venous pressure and rigidity of the upper extremities. The blood pump was stopped. Immediately after the initial symptoms, autotransfusion was initiated while the patient was restless. Eight to nine minutes later, the patient's blood pressure became unmeasurable, which prompted the initiation of cardiopulmonary resuscitation. About 20 minutes later, adrenaline 1 mg was administered by intravenous injection. Despite emergency treatment, the patient died approximately two hours later.

[Abbreviations] Ai = Autopsy imaging (post-mortem imaging); SpO_2 = percutaneous arterial oxygen saturation; JCS = Japan Coma Scale (classification of consciousness disturbance)