

Appendix B

Examples of adverse events associated with unapproved stem cell treatments

| Year | Reported cases | Reported deaths | Patient country of origin | Location of intervention | Condition being treated | Alleged intervention | Administration route | Reported adverse event | Notes |
|-------------------|----------------|-----------------|---------------------------|--------------------------|--|---|---|--|-------|
| 2004 ^a | 5 | | Not reported | China | Spinal cord injury | Olfactory ensheathing fetal cells | Spinal injection | Meningitis, CSF pleocytosis, ^b gastrointestinal bleeding, pneumonia, fever, headache ^c | |
| 2005 ^d | 1 | | Israel | Russia | Ataxia telangiectasia ^a | Fetal neural stem cells (SCs) | Direct injection into brain, spine | Tumors in brain, spine originating from donor fetal neural stem cells | |
| 2006 ^f | 1 | | Not reported | Egypt | Acute inflammation of spinal cord segments | Mesenchymal SCs (MSCs), embryonic, and fetal neural SCs | Spinal injection | Acute inflammation of brain, spinal cord that damaged myelin sheath protecting nerve fibers | |
| 2006 ^g | 1 | | Thailand | Thailand | Kidney inflammation due to lupus | Hematopoietic SCs | Injection into renal regions (no ultrasound guidance) | Multiple lesions in kidney, liver, adrenal gland | |
| 2009 ^h | 1 | | U.S. | U.S. (California) | Face-lift | Adipose-derived stromal cells | Injections around eye | Bone-like growth in eyelid | |

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|----------------------|----------------|-----------------|--------------------------------------|--------------------------|---|--|-------------------------------------|---|---|
| 2010 ⁱ | 3 | 2 | Italy; Azerbaijan; U.S. (Ohio) | Germany | Unspecified neurological conditions | Bone marrow-derived SCs | Direct injection into brain | Brain hemorrhage; death | Though the treating clinic in Germany was shut down, provider subsequently opened a similar clinic in Lebanon |
| 2010-12 ⁱ | 2 | 2 | U.S. (Indiana, Florida) | U.S. (Florida) | Leg numbness, difficulty walking after cancer treatment; pulmonary hypertension | Grossly filtered bone marrow aspirate; adipose-derived stromal cells | Different methods of administration | Stroke; cardiac arrest; death in both cases | Provider was subsequently barred from practicing medicine in Florida but continues to treat patients in the Dominican Republic ^k |
| 2011 ⁱ | 1 | 1 | U.S. | U.S. (Nevada) | Spontaneous widening of bronchi (for unknown reasons) | Nonspecified SC intervention | Unknown | Death | |

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|----------------------|----------------|-----------------|--|--|---|---|--------------------------|--|---|
| 2012-14 ^m | At least 10 | At least 7 | Several countries, including U.S. (Illinois) | Italy; Spain; Russia; U.K.; Sweden; U.S. | Various conditions affecting trachea function | SC-coated plastic or cadaveric trachea | Surgical transplant | Pulmonary embolism, postoperative infection, transplant failure; death | Patients were treated by the same surgeon, who was found to have engaged in numerous instances of scientific misconduct |
| 2012 ⁿ | 1 | Not reported | Not reported | Japan | Chronic kidney failure | Adipose-derived MSCs | Intravenous infusion | Unspecified neurological event | |
| 2013 ^o | 3 | Not reported | Not reported | Not reported | Herniated intervertebral disc | Adipose-derived MSCs | Intravenous infusion | Pulmonary embolism | |
| 2013 ^p | 1 | 1 | Australia | Australia | Dementia | Autologous adipose stromal cells | Unknown | Uncontrolled blood loss during liposuction procedure, shock, death | Patient was on anticoagulant medication, which caused uncontrolled bleeding |
| 2014 ^q | 6 | Not reported | Canada, U.S. (New York) | Germany | Not reported | Live cell therapy/fresh cell therapy ^r | Intramuscular injections | Q fever | |

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|---------------------------|----------------|-----------------|---------------------------|--|--|---|---|--|---|
| 2016-17 ^s | At least 5 | | Not reported | U.S. (California, other locations not specified) | Various conditions including chronic obstructive pulmonary disease | Adipose-derived stromal cells | Infusion, direct injection into brain, knee, and eyes; inhalation | Loss of consciousness, headaches, confusion, inability to walk, infection, retinal detachment, hospitalization | These adverse events occurred at several affiliated clinics |
| 2018 ^t | 13 | | U.S. | U.S. (Texas, Florida, Arizona) | Various conditions causing joint and back pain | Umbilical cord blood-derived SCs | Injection or infusion | Acute bacterial infections of spine, bones, joints; abscesses; hospitalization | |
| 2018 ^u | 1 | | Not reported | U.S. (Florida) | Arthritis | Not reported | Injection | Vomiting, hospitalization, coma | |
| Not reported ^v | 1 | | U.S. | Costa Rica | Multiple sclerosis | Allogeneic cord blood MSCs and autologous adipose-derived stromal cells | Spinal injection, intravenous infusion | Catastrophic demyelinating encephalomyelitis ^w | |
| Not reported ^x | 1 | | U.S. | China, Argentina, Mexico | Ischemic stroke | MSCs, embryonic, fetal neural SCs | Spinal injections | Lesions in spinal cord and surrounding membranes causing lower-back pain, paraplegia, urinary incontinence | |

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|----------------------------|----------------|-----------------|---------------------------|--------------------------|--|--|-----------------------------|--|-------|
| Not reported ^y | 1 | | U.S. | U.S. | Face-lift | Fatty aspirate from abdominal wall in a procedure called "stem cell face-lift" | Facial injection | Necrotizing ^z facial ulcerations | |
| Not reported ^{aa} | 1 | | U.S. | Portugal ^{bb} | Spinal fracture, associated spinal cord injury | Olfactory mucosal cells | Intraspinal transplantation | Spinal mass consisting of large amounts of mucus | |
| Not reported ^{cc} | 3 | | U.S. | U.S. (Florida) | Age-related macular degeneration | Adipose-derived stromal cells | Eye injections | Hemorrhage and possible retinal detachment in both eyes; one year after injection, patients were either completely blind in both eyes or had minimal vision remaining in one eye | |
| Not reported ^{dd} | 1 | | Not reported | Not reported | Heart disease | Autologous "precursor" cells | Direct injection into heart | Ventricular fibrillation; unable to undergo heart transplantation; death | |

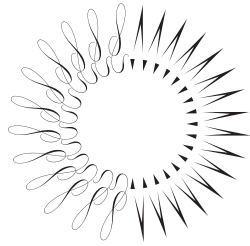
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| Not reported ^{ee} | 1 | | U.K. | Netherlands | Unknown | Umbilical cord blood-derived SCs | Unknown | Serious acute allergic reaction, hospitalization | |
| Not reported ^{ff} | 2 | | Not reported | Japan, China | Different conditions | Adipose-derived stromal cells | Unknown | Pulmonary embolism; death | |
| Not reported ^{gg} | 2 | | China | China | Disabilities from a minor stroke; late-stage liver cirrhosis | Allogenic SCs (not specified) | Spinal, intramuscular injections | Death | Patient with late-stage liver cirrhosis died as a result of being taken off of hepatitis B medication in order to undergo stem cell treatment |
| Not reported ^{hh} | 1 | | Russia | Russia | Aging | Human embryonic SCs | Skin injection | Pea-size facial tumors | |
| Total | 69 | 18 | | | | | | | |

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