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BY

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## IODOFORM POISONING.

BY ELBRIDGE G. CUTLER, M.D.

I. In October, 1876, a lady about sixty years of age came under my charge with cancer of the uterus involving the upper part of the vagina in front and behind. The history was of over a year's duration. The patient was very feeble and confined to her bed. On examination the uterus was found to be fixed, and an indurated nodular crater of considerable size was discovered in place of the cervix. There was much foul smelling, sanguineo-serous discharge constantly, and considerable pain and occasionally hæmorrhage. After exhausting other resources she received suppositories of cocoa-butter containing five grains each of powdered iodoform, one every second day for twelve days (six in all) to diminish the pain and discharge and to change the character of the odor. After a few days the patient became somnolent, the pulse got high, she refused food, and emaciation set in. Soon somnolence gave place to coma, emaciation progressed and she died in collapse thirty-three days after my first visit, ten days after the last suppository. There was a little albumen in the urine (drawn by catheter) but plenty of urea. It was not until some time afterward that I believed that the iodoform had proved poisonous.

II. A few months ago in a congenitally neurotic patient, with post-partum diphtheritis of the vagina and uterus, I introduced six of Mitchell's iodoform uterine bougies, containing five grains each. One was placed in the afternoon of the first day, one morning and night of the next day, and one in the morning of each of the next three days. Within an hour of having the first bougie she complained of feeling faint, and having

a bad taste in the mouth ; the sensations recurred several times in the night. After the second bougie this faintness increased in frequency and was attended with nausea and vomiting. After the fourth she got despondent, tearful, melancholy, was sure she never should recover, and that her baby would die. There was nausea, anorexia, and profuse sweating, and she was very sleepy most of the time. After the fifth, she fainted several times, the pulse remaining, good, full, and about eighty in the minute. She took final leave of her friends preparatory to death, did not wish to recover, and once asked to be chloroformed immediately "and make an end of it." All this time she was getting along well in other respects. She vomited two or three times and slept the greater part of the day and night. After the sixth suppository the faintness recurred and the mental depression increased. As there was no longer any appearance of diphtheritis the iodoform was omitted and the symptoms gradually disappeared. The first to depart was the nausea, faintness and bad taste, afterward the sweating, and lastly the mental depression, which continued the longest. It was fully two weeks after the last bougie before all traces of its action had disappeared.

On a somewhat extended search I have found the following cases of poisoning recorded ; they are all which were accessible to me. The first thirty were collected by Koenig, who was the first to make any extended observations :

(1) Man, aged eighteen, tuberculous abscess above the knee, opened. One gramme iodoform applied. After a few days appearance of symptoms. Delusion that he was being pursued, attempts to leave his bed. Recovery after a few hours.

(2) Woman, forty-seven, carcinoma of breast, amputation. Iodoform and iodoform gauze applied.

Lister dressing. On the fourteenth day the first symptoms began ; they were ill-humor, delusions. Recovery on the twentieth day.

(3) Woman, thirty-two, fistulæ in caries of the ileum, scraped out. Filled with iodoform. Symptoms seventh night, leaves bed, attempts to escape, afterward morose behavior and perverted answers to questions. Recovery (day not stated).

(4) Man, sixty-two, caries of foot, Pirogoff's operation. Iodoform and iodoform gauze, Lister dressing. Ninth day restlessness and anxiety, leaves bed, talks confused nonsense. Recovery on the seventeenth day.

(5) Woman, twenty-four, osteo-sarcoma of jaw, resection. Iodoform and iodoform gauze, then iodoform blown in for seven days. On the eighth day sleeplessness, anxiety, fear of being carried off. Gradual improvement after removal of iodoform.

(6) Man, thirty-five, extensive burn of skin. Every second day powdered with iodoform. On seventh day, "after two dressings," talked confused nonsense, absolutely sleepless, gets out of bed, tears bed-clothes. Recovery about the twenty-eighth day.

(7) Man, sixty-eight, tuberculosis in foot, amputation. Fifty grammes iodoform (in three dressings). Eighth day restlessness, gets out of bed. Rapid disappearance of symptoms.

(8) Man, forty-eight, fracture and dislocation of ankle-joint. Drainage of foot. Sixty grammes iodoform. Beginning on the eighth day there was for three weeks confusion, restlessness, getting out of bed, stupor. Recovery about the twenty-eighth day.

(9) Woman, seventy-two, senile gangrene. Sprinkled with iodoform (thickly). After a time (not stated) temporary lethargy, delirium, defective memory, hallucinations. Death in six weeks later.

(10) Woman, seventy-three, carcinoma of rectum,

operation. Eighty to one hundred grammes iodoform applied, drainage. On the eighth day restlessness, recognizes nobody, does not know where she is, jactitation. Recovery in about four weeks.

(11) Man, sixty-eight, hypertrophied prostate, no operation. Suppository of iodoform and cocoa-butter, then iodoform-vaseline per rectum. Eighth day after using the salve, confusion, delusion of being pursued, gets out of bed, attempts at flight. Recovery "after a few days."

(12) Man, seventy-one, galvanocautistic amputation of penis. Sprinkling of the scab and eight days later the wound with iodoform. Twelfth night, boisterous, during the day refusal of food. Suicidal tendencies. Recovery after "four or five days."

(13) Woman, fifty-four, tuberculosis of foot, curetting of the medullary cavity of tibia. Forty grammes iodoform placed in the cavity. Lister dressing. On the eighth night, confusion and restlessness, afterward hallucinations and refusal of food. Recovery on the eighteenth day.

(14) Woman, twenty-two, ichorous ulceration of the knee-joint, amputation. Iodoform powder and iodoform gauze. Fifty grammes to the eighteenth day. On the nineteenth night attack of insanity, hallucinations. Eight days later severer attack of insanity, distracted. After twenty-seventh day improvement (gangrene occurred later).

(15) Man, twenty-one, arm injured by machinery, at first conservative surgery, then exarticulation. At first forty to fifty grammes iodoform. After operation fifteen to twenty grammes. Two days after operation restlessness, confusion. A few days after the first application of the iodoform, anxiety, afterward insanity. Recovery fifteen days after the operation.

(16) Woman, forty-three, carcinoma of breast, ex-

tirpation. Fifty to eighty grammes iodoform. Lister dressing. Night following tenth day, restlessness, bad language, then insanity, distracted. Death on twenty-first day. (Erysipelas?)

(17) Man, sixty-one, arthritis deformans, resection. Iodoform eighty grammes. Ninth day restlessness, involuntary discharges, stupor, and on seventeenth day maniacal attacks. Death on twentieth day. Collapse, œdema of lungs.

(18) Man, seventy, tuberculous sequestrum of femur, extraction. Ten to fifteen grammes iodoform. Lister dressing. Ninth day delusion of being pursued. Afterward insanity. Death about the twenty-first day (in the third week after the outbreak).

(19) Woman, sixty-nine, extirpation of breast. Iodoform (quantity not stated). Healing by first intention after nine days. On tenth night restlessness, attempts at flight. Seventeenth day maniacal attacks. Involuntary discharges. Death on twentieth day. œdema of lungs.

(20) Man, sixty-one, caries in knee, amputation. Iodoform and iodoform gauze, six days later twenty-five grammes iodoform. On the eighth to the tenth day restlessness at night. During the day sleep, pain; eleventh day hallucinations, afterward refusal of food. death on twelfth day. Collapse.

(21) Woman, sixty-seven, tuberculous elbow-joint. Resection. Ten to fifteen grammes iodoform. Lister. Fourteenth day restlessness, confused talk, refusal of food, afterward attempts at flight during the night. Twentieth day clearer consciousness. Death the twenty-first day. œdema of the pia.

(22) Man, sixty-three, resection of upper jaw. Powdered with iodoform, the following day blown in. Seventh day restlessness, delusion of being followed, hallucinations. Death the twenty-eighth day. Pneumonia symptoms.

(23) Man, twenty-two, complicated fracture of the leg, large incision. Every three days dressing with about fifteen grammes iodoform. Fourth night sleeplessness, restlessness, anxiety; by day rational; loss of appetite, wretched appearance. Improvement after the omission of the iodoform.

(24) Woman, forty-six, struma, extirpation. Iodoform: Lister dressing on the fifth day. Second day repeated vomiting, pulse 164, later more vomiting. On the fifth day dyspnœa, great restlessness, confused talk. Death the sixth day. Œdema of lungs. Autopsy showed fresh pneumonic nodules.

(25) Boy, five, large abscess from coxitis, incision. Sixty grammes iodoform. (Day on which symptoms began not stated). For six weeks somnolence and great perspiration. Recovery after six weeks.

(26) Boy, six, periarticular abscess of the hip-joint, scraped with sharp spoon. Twenty grammes iodoform, then iodoform pencils daily. (Day not given). Apathy, tearfulness, thirst, vomiting, fever, bloody urine. Recovery on eleventh day. Daily change of dressing.

(27) Girl, fifteen, suppuration of hip-joint, resection. Thirty grammes of iodoform, from the fourth day. Lister. Second day vomiting, nausea. Third day flexion contractures. Fourth day sopor. Involuntary discharges. From the fourth day no improvement of the nervous symptoms. Later septicæmia and death.

(28) Boy, fourteen, cheezy abscess of the hip-joint, resection. "Coffee-spoonful" iodoform, iodoform gauze. Second day restlessness, fever, stupor, stammering, and vomiting, and on the third day unconsciousness. Death on the third day. Fatty liver and kidneys.

(29) Man, fifty-one, empyema. Every third day gelatine-iodoform pencils. Cross-grained, iodoform



smell and taste, anorexia, dulness of head. Thirteenth night, insanity and insane ideas, getting out of bed. By day confounding of known people. Recovery on the sixteenth day.

(30) Man, forty, stretching of sciatic nerve. After sixteen days iodoform. After two days sleeplessness and increasing restlessness. Seventh to ninth (?) day insanity, getting out of bed. Recovery on the sixteenth day.

(31) Man, sixty-one, iliac sinus after operation for hernia, incision. Three days iodoform on lint, then blown in for twenty-one days. Third day emaciation began. Nineteenth day low feeling, anorexia, dull, heavy, drowsy, disinclined to move, wandering at night, emaciation. Twenty-third to thirtieth day tongue dry, brown, emaciation, pulse 130, temperature  $101.6^{\circ}$ , hebetude, exhaustion. Three weeks later recovery out of hospital. Iodoform omitted at discharge.

(32) Man, thirty-eight, extensive burn. Iodo-vaseline after four days. Second day pulse and temperature increased. Sixth day delirium, pulse 130, temperature  $101.6^{\circ}$ , weak. On tenth day restlessness, attempts to pull off bandages and bed-clothes. On following days symptoms continue, emaciation, temperature decreases, pulse increases and is feeble. Symptoms last till end of sixth week when coma came on. Death at end of seventh week. Autopsy shows petechiæ over left lung and posterior surface of heart, congested lungs and broncho-pneumonic nodules.

(33) Child, four, extensive burn. Iodo-vaseline on lint. Second day sleepless at night, screaming suggestive of meningitis; drawing up of legs, intense headache. Temperature  $104.6^{\circ}$ , pulse 160. Screaming continued, grinding of teeth, unconsciousness, extremely restless, eyes twitching and rolling during the next three weeks, rapid pulse. Iodoform then omitted.

Recovery complete on the twenty-second day after omission.

(34) Boy, eleven, lumbar abscess, incision, caries of spine. Wall of abscess wiped out with a sponge filled with iodoform. Drainage tubes. Iodized wool dressing. Third night restlessness, rise of temperature ( $104.6^{\circ}$ ) and pulse 138. During the next two days vertical headache, drowsiness, nausea, smell of iodoform in breath. The wounds then washed out with carbolic wash and carbolic gauze substituted for iodoform gauze. Recovery by twenty-fifth day.

(35) Woman, adult, chronic inflammation of middle ear, local application. Small ball of cotton dipped in powdered iodoform and applied, reapplication after twenty-four hours, renewed in three days. Within twenty-four hours dizziness, drowsiness increasing by fourth day to a very marked degree, pulse almost imperceptible, breathing very slow and superficial, fainting. Iodoform washed out. Perfect recovery on the second day.

(36) Man, sixty-two, white swelling of knee-joint, scraping out of fistulæ. Twenty grammes iodoform put in fistulæ. Iodoform wadding, changed on fourth and eighth days with fresh application of ten grammes iodoform. Ninth night delirium, pain in knee, temperature  $101^{\circ}$  nearly, iodine reaction in urine, urine passed in bed. Two days later completely unconscious, refused to swallow and bit teeth together on attempts to feed him, tightly closed eyes on attempts to open same, contraction of neck muscles on attempts to move head forward, forearms convulsively contracted, twitchings in arms, increase of pulse and temperature to  $140$  and  $103^{\circ}$  respectively, sopor. Death on the twelfth day. Autopsy shows lepto-meningitis and splenic tumor.

(37) Woman, fifty-eight, cancer of breast, amputa-

tion and removal axillary glands. Iodoform gauze dressing, six grammes iodoform dusted in the wound. Third day apathetic, complains of feeling bad on being loudly addressed, appetite poor, tongue coated. Iodine reaction in the urine intense. Increase of somnolence and apathy. Trembling movements of hands, attempts to brush things away from face, pulse 120 to 130, temperature normal. Anorexia, pupils do not react, restlessness, increasing weakness, sopor. Death twenty-three days after the operation. Pia injected, œdematous, fatty liver, cloudy kidneys.

(38) Man, eighty-two, carcinoma at angle lower jaw, removed. Four grammes iodoform powder covered with wadding. Second day very restless, excited, tries to get out of bed, answers only on loud calling, complains of great headache, thirst; next day unconscious, jactitation, muscular twitchings of face. Fourth day pupils contracted, pulse 130, temperature  $100.1^{\circ}$ , occasional convulsive movements of the upper extremities. Fifth day involuntary discharges into bed, no iodine salts or albumen in urine. Great weakness and emaciation. Death on sixth day after the operation.

(39) Man, fifty-seven, tuberculous ostitis of ulna, resection. 150 to 200 grammes iodoform packed into wound. Lister. Second day large quantity of iodine salt in urine, frequent pulse, excited, restless, delirium at night suggestive of delirium tremens, gets out of bed. Third day strikingly quiet, lies for hours motionless, gives perverted answers to questions with stammering speech, urine and fæces passed into bed. Fourth day hard to rouse, small frequent pulse, neck muscles stiff. Seventh day unconscious, pulse and respiration more rapid, appearance of œdema of lungs, coma. Death on the ninth day. Slight chronic leptomeningitis. Fatty degeneration of heart, kidneys and liver.

(40) Woman, sixty-three, periarticular abscess of left knee, incision, curetted. 100 to 150 grammes iodoform. Lister. Fourth day great headache, depression, loss of appetite, malaise, pulse quickened, temperature normal. Ninth day iodine reaction in urine. Eleventh day depression increased, constant somnolence, answers at random or not at all, urine involuntary. Twelfth and thirteenth day apathetic; difficult to rouse, lips or stammers in answering, next day more comatose, stools and urine involuntary, temperature rising, symptoms continue to sixteenth day when there was œdema of the lungs. Death on sixteenth day. Heart muscles very flabby, spotted yellow and reddish brown, fatty degeneration of epithelium of cortex of kidneys.

(41) Woman, sixty-one, double kolporrhaphia with perinæorrhaphia. Three to four grammes iodoform, strip of gauze. Third day (sixty hours) refuses food and medicine, fears poisoning, tries to get out of bed, delirium later, bites, scratches, cries out, hallucinations of sight, sleepless. Fifth day pupils narrow but react, thumbs turned in, neck stiff, mouth tightly closed, trismus exists, face strongly congested, eyes prominent and bright. Sixth day marked stiffness of neck, regular beating with the forearms, temperature  $101^{\circ}$ , pulse 80 full and strong, collapse in night, death. Death on the sixth day. Atrophy of one kidney, sclerosis of vessels of brain which presumably acted as predisposing conditions of poisoning.

(42) Boy, fourteen, chronic abscess in front of hip-joint, opened sinus. Washed out with ethereal solution of iodoform, iodoform and encalyptol bougies introduced every second day each containing five grammes. After a few days great depression, nausea, vomiting, pulse rapid and feeble 130 to 160, frontal headache, dull mental state, dull pain in epigastrium, emaciation,

irregular pyrexia. Nine bougies used (about 5.0 grammes). Recovery in three weeks.

(43) Man, twenty-four, laryngeal phthisis. .06 grammes iodoform blown in daily. Thirtieth day irregular and intermittent pulse, fulness at stomach, faintness, exhaustion. Recovery immediate on leaving off iodoform.

(44) Woman, young, ecthymatous ulcerations. Scabs removed on head, surface sprinkled with iodoform powder. In a few hours scalp and neck swollen, quick pulse, nausea, restlessness. Recovery on seventh day.

(45) Woman, forty, syphilitic ulceration under chin. Ointment of one gramme iodoform to thirty, applied on lint. Ninth day face red and swollen, covered with vesicles. Twelfth day temperature  $102^{\circ}$ , delirious, weak and irregular pulse. Recovery on sixteenth day.

(46) Man, twenty-three, abscess under shoulder-blade. Iodoform 15.5 grammes applied in sinus in seven days. Seventh day delirious, temperature  $104^{\circ}$ , pulse 120, soon unconscious, stupor, pupils dilated, sphincters relaxed, sleepless, attempts to throw off bed-clothes, impaired muscular power, does not understand spoken words, symptoms lasted five days. Urine scanty, 1036 specific gravity, concentrated, no albumen or sugar, iodine reaction. Recovery on the eleventh day.

(47) Woman, forty, cancer of breast, secondary operation undermining skin. Twenty-five grammes iodoform powder strewn over wound and under flaps. Lister. Second day restless night, face very red, peculiar brightness in eye, pulse 110; next day very much excited, restless, cries out, spits all round herself, refuses food, constantly tries to pull off the bandages, appeared like one with acute mania, albumen and iodine in urine. The next few days unless under

the influence of morphia, raved, tried to get out of bed, spat about, pulse 120 to 130, temperature 102°. Death on the ninth day.

(48) Woman, aged forty, ovariectomy (carcinoma). Partial removal. Twenty-five grammes iodoform powder put in the abdominal cavity. Lister. In one hour the temperature became 101.5°, patient became somnolent, feeble pulse, respiration very frequent and superficial, sweating, sleepless night, vomited, very restless, thirst, pulse 140, respiration 32, pupils contracted. Next day same, iodine in urine. Death at night of third day with symptoms of dyspnoea.

(49) Man, forty-eight, sarcoma of thigh; amputation; drainage-tube. Drainage-tube rolled round in iodoform powder and placed. Renewed in two days. Second day, pulse 120, temperature normal; recognizes no one, does not know where he is; tries to tear off dressing, picks at bed-clothes, attempts to jump from bed. Symptoms last five days. Gradual recovery after the fifth day.

(50) Woman, fifty-eight, extirpation of rectum. A little iodoform rubbed into the cavity of the wound. Second day, restless at night; constantly talking, hallucinations; pulse rapid; end of week, loss of consciousness. Symptoms last three weeks. Recovery gradual after three weeks.

(51) Boy, of three; necrosis of tibia, operation. Wound filled with iodoform; dressing changed three times. After a time (day not stated) there was high fever, somnolence; on the skin of the body, flexor surfaces of both arms, and the inner surfaces of the thighs, a diffuse, bright red color, disappearing under pressure; islands of normal skin. Iodine, albumen, and epithelial casts in the urine. Recovery in three days. Renewal of treatment in a month brought on the same symptoms. The patient gradually became accustomed to iodoform, and was dismissed cured.

(52) Man, thirty-six, caries of rib; operation. Iodoform pencil in sinus every second day. On the tenth day, itching of the extremities; next day, urticaria nodules on the skin of the body and the extremities, from the size of a lentil to that of a three-cent piece, and of red color. Iodine in the urine; no albumen. Recovery.

(53) Woman, fifty, recurrent carcinoma of breast; operation. Thick layer of iodoform powder, nine inches long, reapplied after four days. On the tenth day, delirium at night, unconsciousness, patient emaciating, pulse weak, frequent, no fever, constant delirium, refuses food. Eleventh day, temperature  $101.5^{\circ}$ , collapse, death two days later. Death on the thirteenth day.

(54) Woman, of forty, collection of pus in knee-joint; incised, abscess in popliteal space and thigh, incision, drained. After two days, iodoform powder in wounds, and two pencils in sinuses (one gram. each). After a time (not stated), delirium, anxiety, idea of being followed, hallucinations, emaciation, feeble, rapid pulse, high fever for three days. Recovery in a few days.

(55) —(?) Empyema necessitatis, incision. Lister. Pencil of two-grm. iodoform inserted twice. On seventh day, delirium, maniacal, pallor, anxiety; must be confined in a canvas jacket; temperature  $101^{\circ}$ , feeble pulse. Recovery in three or four days.

(56) Woman, of twenty-six, gummata on head and clavicles, ulceration, necrosis. Pills of iodoform 0.1 each (two to four daily), internally up to 42.0 grms. and unguentum iodoform, one part to ten, applied indefinitely. On the eighth day feels faint and weak on legs, double vision, lasting two and a half days, then vomiting, deep sleep, anorexia, lasting two days; then loud outcries, getting out of bed, confused talk, ina-

bility to seize and hold objects, double vision, headache. Symptoms improve, but last nine days. Recovery gradual after ninth day.

(57) Woman, sixty-nine, syphilitic necrosis of hard palate. Iodoform pills, 0.1 grm. each, two to four per diem (5.0 grammes had been taken in seven days). On the eighth day, somnolence, does not know what she says, walks clumsily and uncertain, like a drunken person; sleepless at night, headache, coma two days later, occasional incontinence of urine, which contains iodine, mild delirium, gets out of bed. Recovery gradual after the twelfth day.

(58) Woman, sixty-six, cancer of rectum; excision. Iodoform powder applied with finger to wound; iodoform gauze. In about thirty-six hours, cloudy sensorium, answers merely "yes" to all questions, difficult to feed, temperature normal, urine drawn by catheter, normal. In the night crying out; tries to get up. Next day, symptoms more intense; urine cloudy, contains enormous quantity of albumen, dark and transparent casts, epithelium, pus, fat drops. Later, iodine reaction in urine. Next day, restless, soporific, weak pulse (Pilocarpin injection, followed by much sweat and saliva; latter and urine contain iodine). Stiffness of extremities on attempting to flex them, extension easy; tracheal râles. Next day condition worse, pulse weak, intermittent, and irregular, cyanotic color, cold sweat. Transfusion, two hundred grams. blood, no reaction. Death on the fifth day. Autopsy reveals nothing.

(59) Woman, forty-seven, sarcoma of thigh; excision. Iodoform gauze on third and seventh day, and on eighth day iodoform placed in wound. Gauze renewed thrice. On the sixteenth day, pupils dilated, pulse 164, passes fæces in bed, feels bad. End of day, jactitation, cries out, groans, speaks indistinctly,



pulse very small, respiration very rapid; *transfusion of solution of common salt, 500 grams.*; pulse improves in strength; rate, as before, 160; continues very restless, and cries out terribly; early next morning have to apply canvas jacket; refuses food. Next day, fed by tube. Gradual improvement and recovery on fourth day.

(60) Man, forty-three, caries of rib; excision. Iodoform powder (amount not stated) to wound. Tenth to twelfth day, lassitude, anorexia, vomiting, diarrhœa; temperature normal, pulse rapid. Soon delirium, springing out of bed; tears off dressings, hallucinations, urine contains albumen and much iodine. Iodoform removed; delirium ceased, but patient remained lachrymose and rapidly emaciated. Death on — day with dropsical symptoms.

(61) Woman, forty; lupus in face curretted. Iodoform powder (quantity not stated) to wound. In a few hours, vomiting, headache, nausea, iodoform smell and taste, diarrhœa, anorexia, lachrymosity, sensorium free, sleepless, rapid and striking loss of strength, pulse small and rapid, temperature  $101^{\circ}$  to  $102^{\circ}$ , urine contains iodine, removal of iodoform. Recovery in thirty-eight days. Recurrence of symptoms on renewal of treatment.

(62) Woman, twenty-four and a half, chronic uterine inflammation; six grams. iodoform (daily, .1 for sixty days) in the vagina. At length (day not given) depression, pulse 120, sopor. for three days; then excitation, gets out of bed, delirium, confusion, lasting some days. Recovery gradual.

(63) Man, twenty-one, suppurating glands in groin after urethritis; opened. Iodoform dressing for eight days. On the ninth day, temperature  $102^{\circ}$ ; headache, somnolent, restless, dreams; omitted dressing; recovery. Renewed dressing, same symptoms. Recovery in few days.

(64) Man, fifty-eight, blow on head, wound five centimeters long. Wound filled with iodoform powder. On the tenth day, some fever, anorexia, headache, lasting several days; then confused, talking nonsense, attempts to escape; mania later. Quick pulse, iodine in urine. Iodoform omitted and bicarbonate of potash given internally. Recovery complete in seven days.

(65) Man, thirty-six, amputation of leg for diseased ankle. Lister. One week later, iodoform powder sprinkled on for four days, then syringed out with iodoform ether once. On the thirteenth day, breathlessness, anorexia. In the night, unconscious, by day absent-minded; tremor, temperature normal, pulse small, 120; strong iodine reaction in urine; next night escapes from bed; diminished consciousness. Recovery about the nineteenth day.

(66) Boy, of three, resection of hip; chiselling out acetabulum. Cavity washed out with saturated solution of iodoform in ether; then Lister dressing and sublimate gauze. Week later, again washed out and iodoform powder put in. In a few hours from the first application, vomiting, lasting fourteen days; great quantity of iodine in urine, little appetite. Hallucinations of sight by night, less frequent by day. Much emaciation; gradual improvement. Recovery from poisoning after a few weeks. Death from the disease some nine months later.

(67) Man, seventy-two, exarticulation for caries of toe-joint. Iodoform powder applied (small amount). On the eighth day, headache, melancholia; next day, excitation, getting out of bed. Recovery in eight or ten days.

(68) Man, old, crush of hand. Considerable iodoform powder, bound up with charpie. In a "few days," restlessness, confusion of thought, talks nonsense. Recovery shortly (not stated when).

(69) Woman, fifty-six, cancer of breast; extirpation. Iodoform powder (no statement of amount given). On the ninth day, "symptoms similar to meningitis," somnolence. Death on twentieth day. Fatty degeneration of heart, kidneys, liver; œdema of brain.

(70) Woman, fifty-two, cancer of breast; extirpation. Eight to ten grms. coarse crystalline iodoform inside, ten grms. outside. Dressing changed five times; Lister. Before the third day no appetite, refuses food. On third day, sopor, small pulse, moderate fever. Iodoform omitted ninth day; unconscious, cries out very much, excitement alternates with sopor; emaciation. Death on the thirteenth day. Œdema of pia, fatty degenerated liver, cloudy kidneys, granular heart muscle.

(71) Woman, thirty-seven, amputation of breast. Ten grms. iodoform, iodoform gauze. On the fourth day, delirium by night, weakness of memory by day, apathetic. Eighth day, excited, delirious, involuntary urine and fæces. Eleventh day, unconsciousness, thready pulse, exanthema of small, red spots on whole body, diarrhœa. Death on thirteenth day. Fatty degeneration of heart, liver, and kidneys.

(72) Woman, fifty-eight, amputation of breast. Ten grms. crystalline iodoform. Third night, restlessness, delirium, does not recognize attendants; symptoms continue and increase by day, gets out of bed. Sopor, thready pulse. Death on (?) day. Fatty degeneration of heart, kidneys, liver.

(73) Woman, forty, carcinoma of breast; parts of sternum and ribs removed. Twenty-five grms. powdered iodoform in wound. On the second day, after an unquiet night, acute mania in the morning, tears off bandages, escapes from bed, spits, cries out, refuses food; temperature 102°, pulse 120 to 130. Death on the ninth day.

(74) Woman, forty, carcinoma of ovary; partial removal. Twenty grms. crystalline iodoform to pedicle. Symptoms began on the first day with languor, somnolence, great restlessness, constant talking. Death on third day.

(75) Woman, forty-one, echinococcus of liver; opened. Fifteen grms. crystalline iodoform put in cavity. After twelve days, iodoform gauze. About the third week, great restlessness, dyspnoea, crazy ideas. Death in the fourth week.

(76) Woman, seventy, carcinoma of breast; amputation. Iodoform (amount not given) strewed on wound several days. After a few days, insane ideas. Rapid recovery after washing out iodoform.

(77) Woman, of fifty, carcinoma of breast; amputation. Iodoform (amount not stated) strewed into a place where secretion was retained a few days after operation. On the same day mania began, and lasted for eighteen days. Recovery after the eighteenth day.

Of these cases, the first thirty, as before stated, were reported by Koenig; also cases 49 and 50. Cases 31 to 34 are by Beck, 35 by Bermann, 36 and 37 by Czreny, 38 by Langsteiner, 39 and 40 by Henry, 41 by Schwarz, 42 by Clark, 43 by Coomes, 44 by Fifield, 45 by Goodell, 46 by Hayes, 47 and 48 by Hoeftmann, 51 and 52 by Zeissl; 53, 54, and 55, by Lingen; 56 and 57 by Oberlaender, 58 and 59 by Kocher, 60 and 61 by Pick, 62 by Seeligmüller, 63 by Schiffmann, 64 by Behring; 65, 66, 67, 68, by Kramer; 69, 70, 71, 72, by Hoepfl; 73, 74, 75, 76, 77, by Falkson.

Most of the cases of poisoning by iodoform recorded have followed its application to wounds, but it has also resulted from internal administration (as is seen in the accompanying table, cases 56 and 57, by Oberlaender where 42.0 grammes were taken in eighty days and 5.0 grammes in seven days respectively), as

well as when introduced into the vagina or rectum and when applied to the skin.

The symptoms observed have sprung from disturbances of the heart and brain more especially.

That the physical qualities of iodoform cannot be essentially different from iodine is seen from the fact that it contains 96.47 per cent. of iodine.

*Animals.* Experiments which have been made on animals with iodoform especially by Binz<sup>1</sup> Hoegyes<sup>2</sup> Moeschott<sup>3</sup> Moeller, and Hoepfl seem to bear out this belief. The symptoms which Binz and Moeller obtained after exhibiting large doses were hypnotic action, emaciation, fatty degeneration of the liver, heart, kidneys and lung epithelium. In the subcutaneous injection of iodoform the mucous membrane of the stomach was one of the first organs to be injured. Hoegyes observed besides the symptoms just mentioned, hæmorrhages into the lobes of the lungs. Death occurs with the appearances of general paralysis, according to Binz, special paralysis of the respiratory centre. Falkson<sup>4</sup> experimented by placing the iodoform in the peritoneal sac. He distinguished an acute and a chronic form of poisoning. In the acute the animal is languid, trembles a good deal, is sleepy, has no appetite, occasionally vomits, and has a disturbed gait. The somnolence increases to coma, respiration and the heart's action are quiet, the latter may be quickened, reflex excitation is retained in the coma, epileptic attacks frequently occur with marked opisthotonos. There is a decided loss in weight. An intermediate stage of apparently perfect health is seen between the operation and the beginning of toxic symptoms (in dogs),

<sup>1</sup> Archiv. für experimentelle Pathologie und Pharmakologie Band, viii und xiii.

<sup>2</sup> Archiv. für experimentelle Pathologie und Pharmakologie Band, x.

<sup>3</sup> Wiener Medicinische Wochenschrift, 1878.

<sup>4</sup> Archiv. für Klinische Chirurgie, 1882, xxviii, 112-156.

which shows that a certain cumulation of the poison occurs in the blood and tissue-fluids before these symptoms come on. This stage sometimes covers a period of several days.

In the chronic poisoning the preliminary stage of health lasts longer. The first symptoms are diminished appetite, with vomiting and increased thirst, then occur languor, indisposition to move, anger at being disturbed, nasal catarrh, dyspnœa, irregularity in the urinary secretion, albumen in the urine, emaciation, trembling of the muscles, coma, difficult respiration. The result of his autopsies was similar to that of the above observers. He found that the iodoform might become encapsulated in the peritoneum just like any other foreign body, but its resorption was not thereby stopped. This same encapsulating was found to occur by Gussenbauer in some of his patients.

*Human Subject.* The toxic symptoms caused by iodoform in human subjects are very much the same as those obtained on experimentation with lower animals. A narcotic soporific action is observed and a considerable increase in the frequency of the pulse, 130 to 160 beats or more. These symptoms are not serious but sometimes very grave ones occur which may lead to a fatal issue. In some cases "aseptic fever," so-called, has been observed with a temperature of 103°, and death with a clear sensorium. More frequently, severe brain disturbances occur either with the picture of an acute meningitis or true mental disease which may be followed by death, even when the drug has been discarded. Autopsy in such cases has given fatty degeneration of internal organs, especially the liver. Sometimes very severe and lasting attacks of diarrhœa have been observed.

It has been found that in factories where iodine preparations are manufactured the employés suffer

from acute, subacute, and chronic poisoning. The acute form is distinguished by severe irritative cough, headache, inflammation of the conjunctivæ and nasal mucous membrane, sometimes also by temporary loss of consciousness. In the subacute affection is comprehended protracted swelling of eyelids, flow of tears, severe frontal headache, frequent sneezing (iodine catarrh). Fever, elevation of temperature, increase of pulse seldom occur in these employés. More frequent than the above are cases of chronic poisoning, so-called iodism, a cachectic condition which develops as the result of frequent and lasting gastric catarrh.

*Symptoms.* The symptoms of poisoning by iodoform in patients show different degrees. Schede made out six degrees, Koenig divides cases into mild and severe, Nussbaum gives three as follows :

(1) The mildest form is that in which the symptoms disappear in a few days after removing the iodoform. They consist chiefly of iodoform taste and smell, patients cease eating, sleep little, are excited, angry, sometimes a little delirious and consider themselves sicker than they really are.

(2) The second degree is distinguished by complete loss of appetite which may increase to absolute refusal of food so that finally patients will not even swallow wine or beer ; when they are persuaded to take food they complain that everything tastes like wood to them. The worst feature is the mental disturbance. There is melancholy and tearfulness, an excitability and despondency which is truly most painful for the patient and the friends. Morphia and chloral sometimes refuse to act. With open eyes patients frequently do not recognize those around them, suddenly spring from bed, will dress and attempt to get away without knowing why or where. They pick at the bed clothes, throw their arms about, are wholly inconsolable, be-

lieve that they will never recover and that they will surely become insane. This wretched condition may last for weeks in spite of leaving off the iodoform, it may make a pause and then come on again although the wounds treated with iodoform have long been healed; indeed this condition sometimes first occurs after healing (encapsuling, see case 19 in table). Finally refusal of food ceases, melancholy gives place to an animated appearance and patients recover.

(3) The third degree, on the other hand, shows itself two or three days after the application of iodoform, there is complete apathy, the patient wholly loses consciousness. From the beginning there is absolute refusal of food, the pulse is rapid and thread-like, respiration is sighing, there is sopor. Patients spring out of bed if they still have the power, cry out in words which are indistinguishable, and lisp or speak imperfectly. They lie for hours without reaction, then again they are unquiet. Morphia and chloral are often of no service. The temperature constantly sinks lower. The wild crying out and throwing about of the arms, picking and tearing at the bed-clothes and dressings, permit us to suppose that patients have most unpleasant sensations. All stimulating means, camphor injections, ether, atropine, strychnia and so forth prove to be wholly fruitless. The removal of all the iodoform is of just as little use. Patients die with the appearance of pronounced collapse after they have been for hours and days even cold and pulseless with stertorous breathing.

These groups include most of the prominent symptoms, individual cases present others which may be mentioned.

Long continued headache is frequent.

Rise of temperature is not unfrequently seen, though severe even fatal cases run their course without it;  $102^{\circ}$  is seldom exceeded.



The pulse is almost always increased in frequency, usually as the case progresses towards a fatal issue it becomes small, easily compressible and weak. It ranges from 110 to 180 or a number which cannot be counted.

The respirations are frequently suspirious, or superficial and rapid.

The tongue may have a brownish coat.

Restlessness and delirium are very frequent symptoms. Involuntary discharges are not rare.

Emaciation is marked usually, especially in the chronic cases and where it is progressive a fatal issue is to be apprehended.

Pallor and a feeling of faintness with a good pulse are not so very rare.

Feeling of weakness, hebetude and sleeplessness accompany the milder cases usually.

Nausea, vomiting and anorexia are extremely frequent.

Papulous and simple erythema of the whole body has been seen; it usually has disappeared rapidly on leaving off the iodoform.

The symptoms are most striking and severe at night usually.

*Chemical changes.* Hoegyès considers that iodoform dissolves in the fatty matters with which it comes in contact, from this solution iodine becomes free and forms with the albumen present iodine albumen which is resorbed. According to Binz and Moeller it is dissolved by the fat, iodine is set free which is changed by the alkali present, into iodides and iodates which again circulate in the blood and act on the ganglion cells of the brain and finally appear in the urine and other secretions as iodide of soda and other iodine organic compounds. They deny the occurrence of the intermediate stage claimed by Hoegyès of iodine albumen.

Behring, who experimented on rabbits, thinks that iodoform acts by abstracting alkali from the organism, that in sufficient doses it may cause the death of the animal by this action, and that one may by a proper exhibition of alkali establish a remarkable tolerance of iodoform.

*Etiology.* It is difficult to explain why the poisoning occurs. Various views are entertained on this point. The manufacturers have been blamed, the article being at first expensive and now cheap, it has been suggested that the iodoform might perhaps be impure. That this is not the case may be inferred from the fact that the best and worst results have followed the use of the drug from the same parcel. Others believe the cause to lie in the variable power of absorption of the tissues and consider that it has an especially injurious action when it comes in contact with much fat because it becomes dissolved thereby. If this assumption were correct we should expect to see very fat persons more susceptible to the drug than others, which has not thus far been observed to be the case. Others again, blame the age of the individual, that is advanced age. Young people are said to bear it well, cases of poisoning are less severe with them because they can eliminate it better, their organs of elimination being more apt to be sound at the start. It is certain that of the recorded cases fewer deaths have occurred under the age of fifty than above it. Idiosyncrasy is a sufficient cause for many. Ludwig thinks that in the circulation of iodoform through the body besides the giving off of iodine there is probably some other organic combination formed which causes the toxic action. Nussbaum<sup>5</sup> believes that probably the concurrence of many conditions causes a liability to poi-

<sup>5</sup> Werth und Gefahr der Antiseptica, Vortrag in der Sitzung des Aerztlichen Vereins zu Muenchen am 12 April, 1882.

soning. He speaks especially of a large fatty wound capable of resorption, degenerated heart muscle and diseased kidneys, and recognizes also in a sick enfeebled organism the most dangerous disposition to iodoform poisoning. Mosetig finally regards the simultaneous application of iodoform and carbolic acid as the chief cause. He always used pure iodoform treatment himself. He washes the wound with clean water, then strews the iodoform powder on it and over it lays charpie free from fat and gutta-percha paper. The carbolic acid, according to him, causes nephritic irritation and that is said to hinder the elimination from the body and so cause poisoning. This opinion has a great deal of probability in its favor, first, because Mosetig in spite of his very extensive use of the treatment (3,000 hospital and 4,000 ambulatory patients), has observed no poisoning at all, and second, because in many of the cases recorded in the above table other disinfectants are stated to have been used at the same time. On the other hand the number of cases where no mention of other disinfectants is made, is very large and there are also many where none such could have been used. We are forced therefore, to the conclusion that the cause is yet to be proved.

Bum arrives at the following conclusions :

(1) Iodoform has a poisonous action when the iodine freed in the organism does not become perfectly combined.

(2) This poisoning will happen where the quantity of iodoform introduced is 1, over large, 2, and in qualitative and quantitative changes of the blood. It is surest to occur where these two forces work together.

(3) The use at once or in short intervals of very large quantities of iodoform, especially in anæmic, very young and old individuals is to be avoided.

(4) The iodoform dressing is to be changed as sel-

dom as possible in order to avoid a cumulative action, (and at the same time the iodoform is not to be removed the wound washed and fresh powder or other form applied, as a surface the best suited for absorption is left.)

(5) The iodoform in the wound must never be exposed to a strong pressure as it aids absorption; the dressing is therefore never to be applied tightly.

*Absorption.* With regard to the absorption of iodoform Zeller<sup>6</sup> found that the solubility of iodoform in water was the same as in blood-serum, that is, 0,212 grammes to 1,000 grammes water. Resorption from the stomach was very slow (shown by determining the quantity of iodine eliminated in the urine), that from the peritoneal surface very rapid, and that from the surface of wounds could not be reckoned. Falkson found that even dry crystalline iodoform was absorbed through the intact skin. He made four experiments on different individuals by strewing crystals of iodoform on the forearm and covering it with dry charpie free from fat and gutta-percha paper. After twenty-four to forty-eight hours the urine gave the iodine reaction distinctly. The arm on removing the bandage was always perfectly dry. General testimony seems to prove that a granulating surface will absorb it more readily than a fresh wound, a serous membrane quicker than a muscle-wound, a freshly-sawed bony surface easier than a sequester-capsule, a serous surface in normal condition better than a thickened inflamed one. It is absorbed very readily from the vagina. When applied to a wound by the finger or rubbed in, absorption seems to be almost certain.

*Detection in Urine.* If the iodine reaction is not obtained in all cases in the urine where iodoform is

<sup>6</sup> Versuche ueber die Resorption des Iodoform. Congress of German Society of Surgery in Berlin, June, 1882.

employed it certainly is obtained in all degrees of poisoning. In some severe cases there is albumen and perhaps casts in addition.

(1) To detect iodoform or rather iodine in the urine, the compound is to be first decomposed by fuming nitric acid and dilute sulphuric acid, then a little starch paste and a few drops of bisulphide of carbon are to be added, whereupon a beautiful blue color occurs. On shaking it about, a small portion of the iodine is dissolved by the bisulphide of carbon and a dark-blue ring of iodide of starch is formed on the layer of bisulphide of carbon.

(2) A second though less reliable method is as follows: After starch paste and dilute nitric acid have been added to the urine a few drops of fuming nitric acid are added, when a blue color occurs which on heating disappears and returns again on cooling.

(3) By a third method, after sulphuric acid and fuming nitric acid have been added the fluid is shaken with chloroform. There occurs through solution of the iodine in the chloroform a violet color.

(4) Sometimes the iodine is in such combination that the above reagents do not free it, chlorine water may then be added for this purpose, as I learn from Professor Hills, or the urine may have to be incinerated and then tested (Harnack).

*Pathological appearances* are not constant.

Fatty degeneration of the heart muscle, cloudy swelling of the renal tubular epithelium and fatty degeneration of the liver have been reported not unfrequently; sometimes gastritis has been seen. Croupous pneumonia has been observed by Aschenbrandt in lower animals after inhalations and "pneumonic symptoms," by Koenig, Case 22 (no account of autopsy). In this latter case and in Cases 24 and 32 of the table the suspicion is well founded, I think, that the appear-

ances were probably due to inspiration of foreign matter from the wound or of particles of food. Œdema of the lung has been several times observed. Sometimes there has been œdema of the meninges or brain. Harnack found that certain organs of the body, namely, the brain, contained disproportionately more iodine than others, as the liver and kidneys, and curiously enough, this was found far more abundantly in the cerebellum.

*General Remarks.* With regard to the age of the individual the table shows that of seventy-seven cases of poisoning, twenty-six were under forty years, about one third, and that of the fatal cases, twenty-nine in number, all but two were under forty. A larger number of cases might materially alter these figures.

There seems to be no maximum dose of safety from symptoms; one gramme has given rise to grave consequences and even from a minute amount as in Bermann's case, number 35, in the table, unpleasant results have followed. On the other hand, large amounts 100 to 200 grammes or more have proved harmless.

The smaller the amount of surface covered by iodoform, and the less natural cavities of the body are exposed to its action, or freshly-cut bones, the better is the chance of immunity. Iodoform should never be smeared on or rubbed in, either as powder or salve. No accompanying disinfectant, as carbolic acid or corrosive sublimate, should be used.

*Prognosis.* In youthful persons a quickening of the pulse, 130 to 140 beats in the minute, may last for a long time without any other disturbance following, but if in adults or elderly people free from fever, a permanent and considerable frequency and diminution in strength of the pulse occurs, danger is at hand. If the mental condition gets worse and coma comes on with

collapse the prognosis is grave. Emaciation if progressive is dangerous, but where it remains stationary or slightly diminishes the prognosis is favorable.

*Treatment.* It has been theoretically proposed (Harnack) to give compounds of the alkalies with vegetable acids internally at the first appearance of the symptoms of poisoning, as acetate of potash, and so forth. The object being to furnish the system with abundance of alkali which may combine with any free iodine which may be present. For this purpose the potash are better than the soda compounds, as poisoning has followed the use of the latter.

This course was pursued by Behring in Case 64. If this treatment does not prove beneficial, transfusion of an alkaline common salt solution is suggested, as was successfully accomplished by Kocher, Case 59. Harnack further suggests that the iodoform be washed off the wound with an alkaline carbonate solution, and then with luke-warm water, and that lastly magnesia usta be powdered on.

*Conclusions.* From what has preceded, the following conclusions seem warrantable :

(1) Fresh wounds or unhealthy or tuberculous surfaces are the only ones fitted for the application of iodoform.

(2) Only a thin layer or small amount of iodoform is to be applied.

(3) When granulations appear healthy, iodoform should be omitted and some other non-poisonous substance substituted.

(4) At the first symptom of poisoning, or coincidently with the original use of it, compounds of the alkalies and vegetable acids are to be given by the mouth at frequent intervals, as acetate of potash. If severe symptoms supervene, transfusion with common salt solution is to be resorted to, and the wound is to

be washed free from iodoform with pure water and an alkaline carbonate solution and afterward powdered magnesia is to be dusted on.

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