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The Determination of Polydimethylsiloxane (Silicone Oil) in Biological Materials: A Case Report

Silicones, synthetic organosilicon oxide polymers, are classified as fluids, rubbers, resins, and compounds. In addition to many industrial applications, the fluids (or oils) have widespread use in the formulation of cosmetic and pharmaceutical preparations.

In 1965 the U.S. Food and Drug Administration (USFDA) authorized the use of medical-grade silicone fluid as an injectable prosthesis under carefully controlled conditions [*1*]. However, augmentation of breast tissue was specifically excluded in the studies, and no silicone fluid has been approved for general clinical use in other soft tissue augmentation procedures.[2]

In spite of reports that little, if any, biological response has been demonstrated after subcutaneous, intramuscular, or intraperitoneal injections of polydimethylsiloxanes [*2*], many cases of nonfatal complications following contour restorations with silicone oils have been reported [*3*]. However, it is believed that this study is the only documented report of isolating, chemically identifying, and quantifying silicone oil from blood and internal organs in a case involving death following breast tissue augmentation with the polymer.

Case History[3]

At approximately 3 p.m., J. S., a caucasian female, age 40, was administered injections of silicone fluid in both breasts by a man posing as a medical doctor. This was the fourth time she had received such injections. A friend who accompanied her stated that the procedure was preceded by "injections to deaden the pain." The friend further stated the J. S. had consumed about half of a fifth of whiskey during the day. Following the procedure and while returning to their homes in a city about 85 miles distant, J. S. became unconscious. The friend at first attributed this condition to the alcohol J. S. had consumed; however, she became more concerned when she could not revive J. S. upon their arrival home, and it became necessary to engage the help of neighbors to take J. S. into her house. Her condition continued to deteriorate and J. S. was admitted to a hospital at 10 p.m. According to the clinical abstract in the gross autopsy report,[4] "(the)

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[2] Whitehead, Anthony J., supervising investigator, USFDA, Atlanta, Ga., personal communication, 25 April 1973.

[3] Briefed from the Officers' Investigation Reports.

[4] The autopsy was performed by J. W. Eversole, M.D., chief pathologist, Medical Center of Georgia, Macon, Ga.

patient experienced respiratory difficulty and expired approximately 12 hours following admission without responding to inhalation and medical therapy."

The following excerpts are taken from the gross autopsy report.

> The pupils are equal, round and regular, dilated...
>
> The breasts are full, firm and erect. In the inferior portion of each breast is a single needle puncture wound...
>
> When the incision is made around the breasts a large amount of clear, slick, greasy fluid escapes...
>
> The right lung weighs 800 grams. It is considerably heavier than normal. The right lower and middle lobes sink when placed in water. They are relatively non-air containing by palpation. The bronchial tree contains no foreign material. The pulmonary vessels contain no antemortem clots. The lung parenchyma is edematous, wet in appearance, red in color. The left lung weighs 650 grams. It is heavy, non-air containing. The lower lobe sinks when placed in water. The lung is purple in color...
>
> The brain weighs 1100 grams. It is symmetrical. The pial vessels are injected. The pia is not thickened. There is a small cerebellar cone. The gray and white parenchyma of the brain is without significant alterations. There are no areas of hemorrhage or softening. The cerebellum and pons are without significant alterations.
>
> The heart weighs 280 grams. It is about normal in size. There is no hypertrophy or dilatation. The myocardium is dark brown. There are small focal areas of subendocardial hemorrhage. The epicardium is smooth and glistening. The valves are thin and delicate. The coronaries are minimally atherosclerotic. There are no blood clots present within the right chambers.

The report further states that the spleen, adrenals, kidneys, urinary bladder, ovaries, and pancreas were unremarkable; the uterus had been removed; and the gastrointestinal tract was normal except for the gastric mucosa being hyperemic. Examination of the neck organs revealed the larynx to be "acutely hemorrhagic;" the thyroid gland "non-nodular, dark brown in color and decreased in size;" and the parathyroids not enlarged. No trauma was described.

The report continues:

> Immediately following the gross dissection, frozen sections were performed on lung, liver, brain, and kidney. Vacuoles resembling oil droplets were found within the alveolar capillaries, glomerular capillaries, brain capillaries, and liver sinusoids. Preliminary assumption is that this material probably represents silicone and possibly the cause of death; however, the material needs to be identified more precisely.

The following descriptions, in full, are taken from the pathologist's report of microscopic sections. Descriptions of organs showing no significant pathologic changes are not included.

> LUNGS: Capillary congestion with vacuoles present. Moderate intra-alveolar hemorrhage and interstitial hemorrhage.
>
> SPLEEN: Slight congestion with small vessels containing vacuoles.
>
> LIVER: Vacuoles present in sinusoids. Slight dilatation of pericentral vein sinusoids with slight decrease in hepatic cords.
>
> STOMACH: Moderately severe mucosal congestion.
>
> PANCREAS: A few small scattered intravascular vacuoles.
>
> KIDNEYS: Moderately severe congestion of glomerular capillaries and moderate number of vacuoles in glomerular capillaries.
>
> BRAIN: Multiple scattered areas of vacuoles present within the brain parenchyma without reaction.
>
> BREAST: Few scattered vacuoles.

Experimental

Apparatus

A Beckman IR-20A spectrophotometer was used to obtain spectra of known silicone oil and oil recovered from breast and lung tissue. Instrument settings were those normally used for "Routine Scan": Double Beam; Period, 2; Gain, 5; Scan Speed, 240 cm^{-1}/min.

A Perkin Elmer 305 atomic absorption (AA) spectrophotometer equipped with a PE 165 Recorder and a nitrous oxide burner head (single slot) was used under the following operating conditions:

Direct mode (employing readout meter with zero control)
Range: ultraviolet
Wavelength: 251.6 nm
Slit: 3 (0.3 mm, 0.2 nm)
Source: silicon hollow cathode tube (single element), 25 mA (Fisher Scientific)
Chart speed: 60 mm/min
Aspiration rate: 1.5 ml/min

	Cylinder Regulator, psig	Burner Regulator, psig	Rotameter Settings
Acetylene	15	10	11.5
N_2O	40	30	5

An ARL emission spectrograph with a 1.5-m diffraction grating was used for qualitative identification of silicon in silicone oil following its conversion to SiO_2. Iron standards were obtained from the National Bureau of Standards (NBS) and spectroscopic carbon electrodes were obtained from National Carbon Co., a division of Union Carbide. The ashed samples were sparked for 30 s at 310 V and 3 A. Films were read in an ARL densitometer, Diagram No. 3450.

Reagents

DC® 200 fluid, 350 cSt, industrial grade[5]
Benzene-isopropanol mixed solvent: 15 ml of benzene, ACS reagent, thiophene free, mixed with 85 ml of isopropanol
Methyl isobutyl ketone (MIBK), certified, water saturated
Nitrous oxide, USP anesthesia grade
Acetylene, purified grade, specialty gas (available from Union Carbide, Linde Division)
Octaphenylcyclotetrasiloxane, NBS Reference Material 1066a

Standards

DC® 200 Fluid (350 cSt) was chosen as the analytical standard when it was found to contain 98.5% of the theoretical amount of silicon by comparison to NBS Reference Material 1066a. Solutions were prepared in water-saturated MIBK in concentrations ranging from 10 to 240 μg/ml. In analysis by AA, the lowest concentration gave a reproducible

[5] Supplied by Dow Corning Corp., Midland, Mich. 48640.

response which could be accurately measured, and linearity was achieved throughout the highest concentration.

Procedure

Tissue—Weigh approximately 1 g of tissue into a 20-ml beaker and finely mince with scissors. Rinse any adherent material from the scissors into the beaker successively with small amounts of water, ethanol, and benzene. Place the beaker on a steam bath, evaporate under nitrogen until the tissue is only slightly moist, and transfer to a 40-ml ground-glass-stoppered centrifuge tube. Using accurately pipetted 2.5-ml portions of water-saturated MIBK, thoroughly rinse the beaker twice. Add each rinse to the centrifuge tube. Allow the mixture to stand for two hours with periodic agitation. Centrifuge, remove an aliquot of the upper MIBK layer, and aspirate into the AA spectrophotometer. If necessary, make dilutions with water-saturated MIBK.

Blood or Serum—Pipet 5 ml of blood or serum into a 20-ml ground-glass-stoppered centrifuge tube. Add 3 ml of water-saturated MIBK. Allow the mixture to stand for two hours with periodic agitation. Centrifuge, transfer the MIBK layer into a 12-ml centrifuge tube, and discard the lower aqueous layer. Centrifuge the MIBK solution and aspirate the supernatant into the AA spectrophotometer.

Calculations

Tissue concentrations are determined from a standard curve prepared by plotting micrograms of silicone fluid per 5 ml of MIBK versus chart divisions. Blood concentrations are determined from a similar standard curve using micrograms of silicone fluid per 3 ml of MIBK as the abscissa units.

Recovery Experiments

Specimens of lung tissue were injected with a solution of DC® 200 fluid in benzene-isopropanol mixed solvent in the concentration range from 0.5 to 3 mg%. Analysis of these tissues gave an average recovery of 75%.

Microscopic Sections

Sections of lung, liver, kidney, and brain were prepared using hematoxylin and eosin (H and E) stains, and frozen sections of lung were stained with Sudan 4. Frozen sections were also prepared from specimens of normal lung tissue injected with silicone oil to determine whether or not the polymer would be stained with Sudan 4.

Results and Discussion

Lung, liver, kidney, brain, and serum were analyzed in duplicate according to the procedure. The results are shown in Table 1. No measurable amount of silicone oil could be demonstrated in tissues obtained from unrelated cases.

To confirm the presence of silicone fluid in the lung tissue, the MIBK was evaporated from the extract remaining after AA analysis, and an infrared (IR) spectrum of the residual oil was obtained. Comparison with the IR spectrum of DC® 200 fluid, 350 cSt, is shown in Fig. 1.[6]

[6] No implication is intended that the silicone fluid isolated in this case was Dow Corning® 200 fluid.

TABLE 1—*Results of atomic absorption analysis.*

Tissue	Concentration, mg% (g%)
Lung	4000 (4.0)
Brain	41
Kidney	120
Liver	54
Serum	2.7

In addition to the tissues listed above, breast tissue was also submitted from which an oily liquid was easily expressed. The IR spectrum of this liquid was essentially identical to that of the analytical standard.

The presence of silicon in the oil expressed from the breast tissue was further demonstrated by emission spectrography. Heating the fluid in a platinum dish over a low flame resulted in a light, fluffy, white powder from which the spectrogram was obtained. Eight major silicon lines were identified [*4*].

Silicone fluid in the breast tissue was not quantified.

The serum was negative for alcohol and barbiturates. No drugs were detected in the gastric contents.

Because of the tendency of silicone fluid to adhere to all types of surfaces, it was recognized that losses could be substantial during any handling procedure. In order to minimize such losses, scissors were used to mince the tissues rather than a blender for homogenization.

Immediately before use, all glassware was thoroughly washed in heavy duty detergent and rinsed successively in deionized water, ethanol, and benzene. Glass syringes were used since disposable syringes are lubricated with silicone fluid.

Partial drying of the tissues before extraction with MIBK prevented emulsions, thereby increasing solvent recovery.

In the operation of the AA spectrophotometer, the use of high purity acetylene gas and reduction of the recommended rotameter settings for the gas flows [5] resulted in decreased noise and improved sensitivity.

Under the operating conditions as outlined, the sensitivity of the AA spectrophotometer was 10.6 μg silicone fluid per ml MIBK per 1% absorption, and the detection limit was 4.0 μg silicone fluid per ml MIBK.

The sensitivity of the procedure was 53 μg silicone fluid per gram of tissue, and the detection limit was 20 μg silicone fluid per gram of tissue, without the use of a recovery factor.

Microscopic studies[7,8] of five sections of lung tissue showed zones of massive destruction in which the alveolar walls were ruptured, together with rupture of the capillaries and extravasation of erythrocytes into the alveolar spaces. The degree of pulmonary hemorrhage varied from moderate to marked. In the alveoli which were not ruptured the alveolar spaces were greatly distended. Scattered zones of vacuoles were seen in some of the capillaries (Fig. 2). No fibrosis and no silicosis were observed.

[7] Jones, Herman D., Ph.D. (retired), former director, Georgia Crime Laboratory, Atlanta, Ga., personal communication, 16 Jan. 1974.

[8] Godwin, John T., M.D., chief pathologist, St. Joseph Infirmary, Atlanta, Ga., personal communication, 16 Jan. 1974.

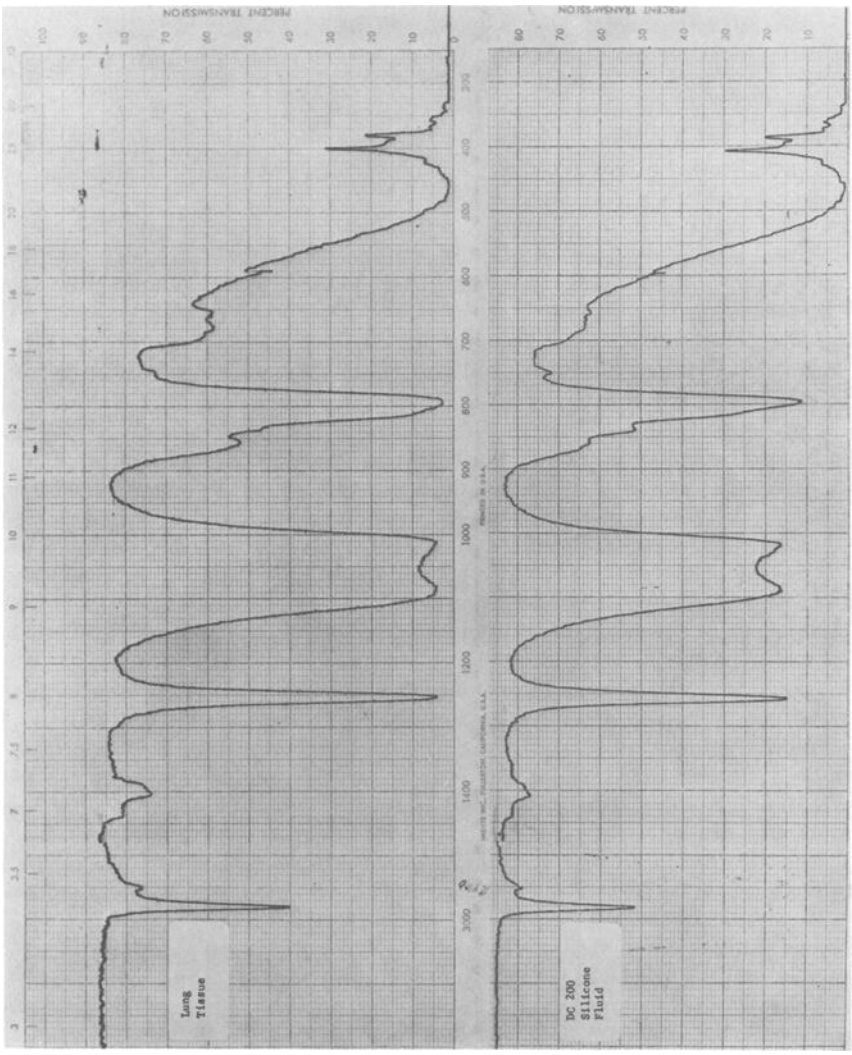

FIG. 1—*IR spectra of oil extracted from lung tissue* (above) *and DC® 200 Silicone fluid* (below).

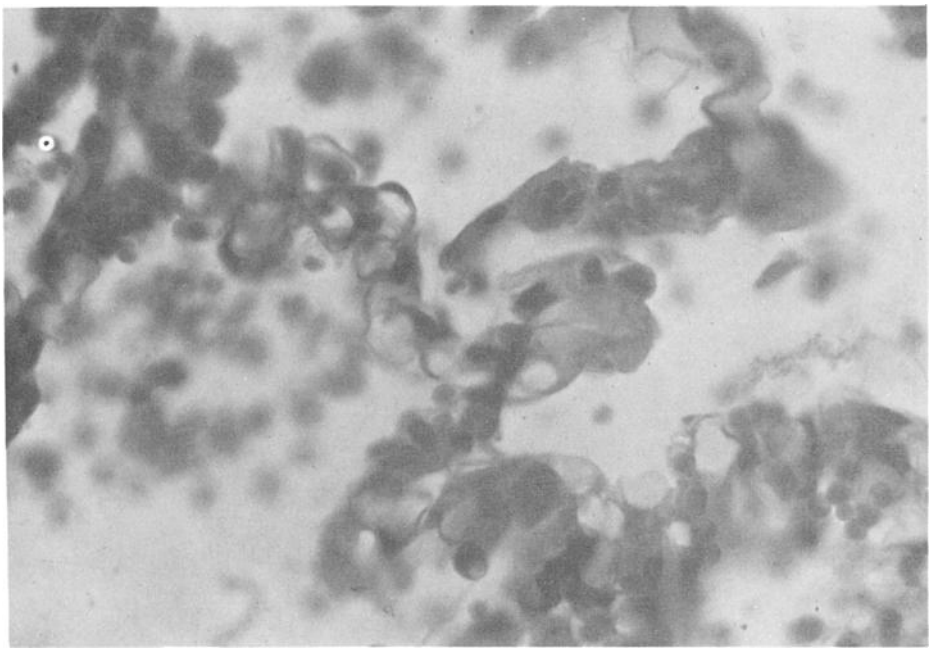

FIG. 2—*Vacuoles resulting from silicone fluid emboli in lung capillaries. Hematoxylin and eosin stain. Original magnification ×400.*

Two sections of kidney revealed the presence of vacuoles in numerous glomeruli (Fig. 3). The number of vacuoles varied from one to eight. Although no vacuoles could be demonstrated in some of the glomeruli, all showed marked vascular engorgement. No arteriolar nor arterionephrosclerosis and no fibrosis was demonstrated. Moderate cellular edema was present in the tubules.

No significant morphological changes were demonstrated in the two sections of liver.

In the limited brain tissue available only two capillaries demonstrated the presence of vacuoles within the lumen (Fig. 4).

Microscopic examination of frozen sections of lung injected with silicone fluid revealed that Sudan 4 would not stain the fluid. Therefore, no conclusions could be drawn concerning the presence of the polymer in similarly stained sections of lung from the case.

Conclusions

Based on (1) a clinical history of the decedent having undergone breast augmentation with silicone fluid; (2) no clinical history of trauma or disease; (3) no microscopic evidence of silicosis or other disease; (4) negative results in the analyses of blood and gastric contents for drugs; (5) recovery of silicone fluid from lung (4 g%), liver, kidney, brain, and serum; and (6) demonstration of emboli in the lungs, it is highly probable that death resulted from pulmonary insufficiency secondary to the presence of a foreign substance, silicone fluid.

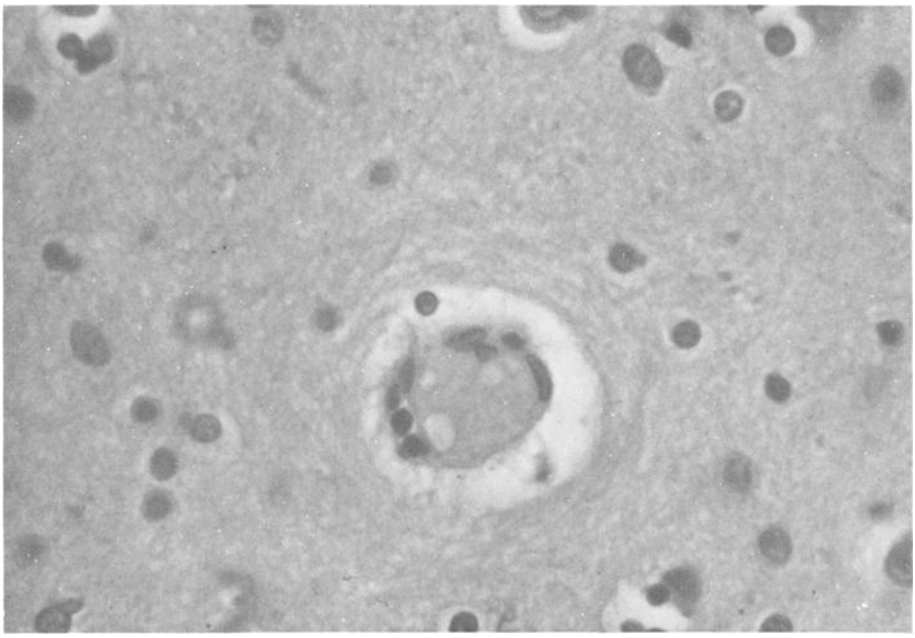

FIG. 3—*Vacuoles resulting from silicone fluid emboli in glomerulus of kidney. Hematoxylin and eosin stain. Original magnification ×400.*

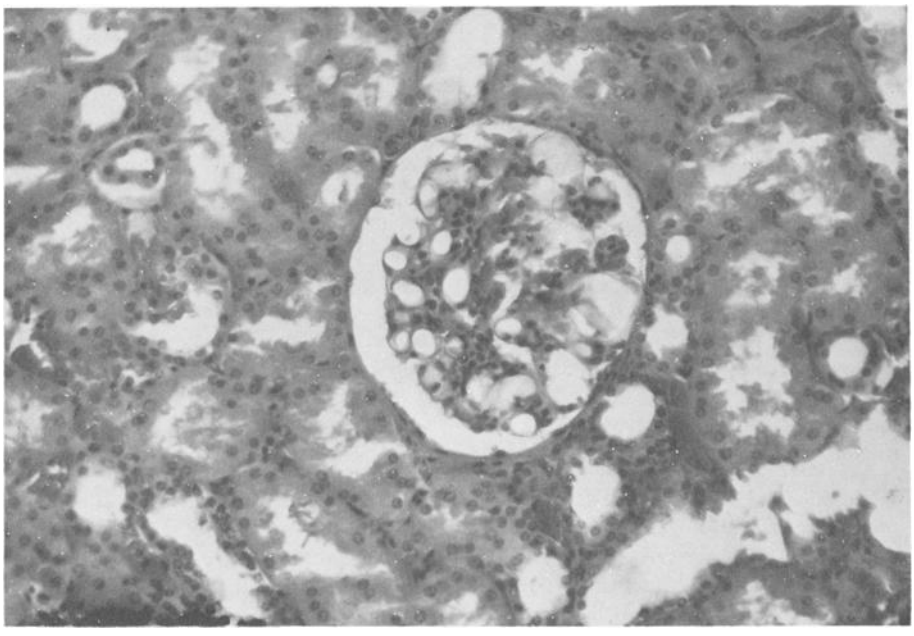

FIG. 4—*Vacuoles resulting from silicone fluid emboli in brain capillary. Hematoxylin and eosin stain. Original magnification ×400.*

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