Serratia marcescens: Masquerader of Blood

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Some strains of S. marcescens are capable of producing pigment, the intensity of which ranges from dark red to pale pink, depending on the age of the colonies. The pigment can be present after incubation at room temperature but usually disappears after subculturing. The pigment was extractred by 1902 and named "prodigiosin" . Serratia marcescens has a predilection for growth on foodstuffs, especially of the starchy variety, where the pigmented colonies were easily mistaken for drops of blood. As early as the sixth century B.C., Pythagoras had noted the appearance of a bloody concentration on foodstuffs, and in the 1800's, Ehrenberg uncovered almost 100 historical references to the miraculous appearance of blood on food.

The first account by classical historians of the appearance of blood on foodstuffs was recorded in 332 B.C. at the siege of Tyre in Phoenicia (modern Lebanon). There, the Macedonian army of Alexander the Great took inspiration from an omen - drops of blood trickling out of the soldiers bread. The Macedonian seers interpreted this dramatic event as prophesying the destruction of Tyre and rallied the previously dispirited army to victory. Tyre was eventually stormed and left ruins. In 541 A.D. at Tours, France, blood trickling from broken bread was said to foretell the defeat of the Lombards as well as the death of the Emperor Tiberius.

Gaughran uncovered more than 35 historical reports of blood flowing from Eucharistic bread, the Host; the first such incident was recorded in 1169 in Denmark. The starchy sacrament incubated in the damp environment of medieval churches provided an excellent substrate for the growth of S. marcescens. Since the Eucharistic bread symbolized conversion into the body of Christ, the appearance of blood on the Eucharistic bread represented a dramatic testament to this dogma. In 1264, a priest in Bolsena, Italy, who allegedly doubted the miraculous view of the sacrament was celebrating mass when "blood" appeared on the Eucharistic bread and dripped onto his robe. This episode was commemorated by Raphael in his fresco "The Mass of Bolsena". Unfortunately, many of these episodes also served as a basis for the persecution of Jews who allegedly stabbed the Host.

In 1819, the source of this miraculous blood was attributed to a micro-organism. At that time, a bloody discoloration of cornmeal mush was observed in an Italian peasant's home. The household not only became distraught by this mysterious visitation but also became fearful of divine vengeance, as predicted by the crowds who flocked to their home. Rumors spread that a supernatural power had caused blood to spring from the polenta because it ahd been made from cornmeal that had been hoarded and denied the hungry during the famine of 1817! Bartoleno Bizio, a young pharmacist, demonstrated that "blood" was caused by a living organism, which he mistakenly believed was a fungus. He named this organism Serratia marcescens. Serratia was named in honor of an Italian physicist, Serafino Serrati, who Bizio thought had been slighted in favor of American inventors as to priority for the invention of the steamboat. Marcescens is derived from the Latin word "to decay" since Bizio observed that the pigment deteriorated quickly, dissolving from a light-pink material into a purplish-red, viscous form. Bizio's experiments were of historical interest because they were one of the earliest instances of the use of solid medium (in this case, cornmeal mush) for the cultivation of chromogenic bacteria. Vincenzo Sette, an Italian physician who also concluded that the red coloration originated from a micro-organism, dispelled much of the mysticism generated by the superstitious populace. By reproducing the reddening of polenta in the house of a priest, he disproved the notion that such an event could occur only in the house of a sinner.

In 1848, Ehrenberg named the organism Monas prodigiosus, or the "miracle bacterium," which was later modified to Bacillus prodigiosus. By the 1920's, revisions in taxonomy of bacteria as well as the desire to recognize the work of Bizio led to the gradual adoption of the name originally proposed by Bizio.

The first clinical report involving S. marcescens was also a result of its pigment production. In 1913, a patient with bronchiectasis had repeated episodes of what the patient considered to be blood-tinged sputum. However, microscopial examination failed to reveal red blood cells but did show a large number of gram-negative bacteria, which proved to be S. marcescens. By 1957, similar cases were reported. The term "pseudohemoptysis" was coined for this syndrome.

In 1958, ‘red diaper syndrome’" was observed in an infant at the University of Wisconsin Hospital. Since the "blue diaper syndrome" is caused by the abnormal metabolism of tryptophan, the father of the infant, a genetics professor, suspected an inborn error of metabolism. Eventually, these workers isolates S. marcescens from the infant’s stool; absorption spectrophotometry verified that the coloration in the diapers originated from the pigment produced by the bacterium. They subsequently discovered that a pigmented strain of S. marcescens was being used as a marker in a study of aerosol technics in a nearby laboratory and that it was antigenically identical to the infant’s strain. The infant was asymptomatic, but, despite sulfasuxidine therapy, his diapers continued to show red coloration for the next seven months.

Use As A Biologic Marker

With the present appreciation of the pathogenic potential of this organism, it is difficult to realize how benign it was once considered to be, and how recently. Indeed, its main claim to fame before its reputation as a nosocomial pathogen was its use as a biologic indicator.

In 1906 M.H. Gordon, after gargling a liquid culture of S. marcescens, recited passages from Shakespeare to an audience of agar plates in an empty House of Commons. He had been commissioned to study the atmospheric hygiene of the House after an epidemic of influenza had appeared among its members. Gordon recovered colonies of pigmented S. marcescens from agar plates, demonstrating that speech, as well as coughing and sneezing, could project bacteria into the air. He reportedly suffered no ill effects from the experiment.

As recently as the early 1970’s, microbiology students rubbed their hands with suspensions of S. marcescens to demonstrate dispersal of bacteria by hand-shaking in routine laboratory exercises. The organism was even sprayed into hospitals to study bacterial drift and settling.

As a result of its use as a biologic marker, S. marcescens played an important part in many classic experiments, leading to an improved understanding of mechanisms of infection in man. In a controlled experiment conducted in 1920 to test the hypothesis

that respiratory-tract infections could be transmitted by hand, the throats, mouths, and lips of American solidiers were sprayed with a suspension of S. marcescens. The organism was subsequently from the hand, mess-kit utensils and oral cavities of other noninfected solidiers.

The knowledge that bacteremia can occur after dental extraction can be partially ascribed to the use of S. marcescens as a marker. In two classic studies, the organism was painted on the gum or neck of the tooth to be extracted, and blood cultures were obtained after tooth extraction. In one study, S. marcescens was isolated from the blood of 41 percent of their patients. None of the subjects were known to have suffered any ill effects.

Kass and Schneiderman documented the entry of organisms into urinary tracts via indwelling bladder catheters by applying S. marcescens to the periurethral epithelium of three patients with indwelling catheters. Within three days, they recovered large amonts of the test organism from the urine of their patients. S. marcescens was to the mouth and pharynx of patients with respiratory-tract infections for use as a marker of contamination of sputum by mouth flora.

The most controversial use of S. marcescens as a biologic marker involved aerosolization experiments conducted by the United States population to study the germ warfare techniques (Table 1). In 1950 and 1952, Navy ships released S. marcescens into the ocean, where the organism became aerosolized by ocean waves and was then blown inland to San Francisco. Monitoring stations isolated the organism from the air as far as 80 meters inland. Public interest regarding the Army experiments was ignited by news reports in December 1976, that a San Francisco hospital had experienced an outbreak of S. marcescens infections coinciding with the aerosolization experiments that had been performed in 1950. Pigmented Serratia was released over cities, in bus terminals, and in subways. (Another "nonpathogenic" organism used in these experiments was Aspergillus fumigatus.

One of the first documented outbreaks of nosocomial Serratia infection occurred in a San Francisco hospital within the time period that Navy ships released massive numbers of Serratia near San Francisco to study wind and water currents. One of the patients infected during this outbreak developed and succumbed to endocarditis-the first case of endocarditis caused by S. marcescens. This revelation was publicized on the

television program 60 Minutes in 1980. Relatives of the deceased failed in their legal attempt to recover damages from the U.S. government because they were unable to make a definitive link to the Army's aerosolization experiments.

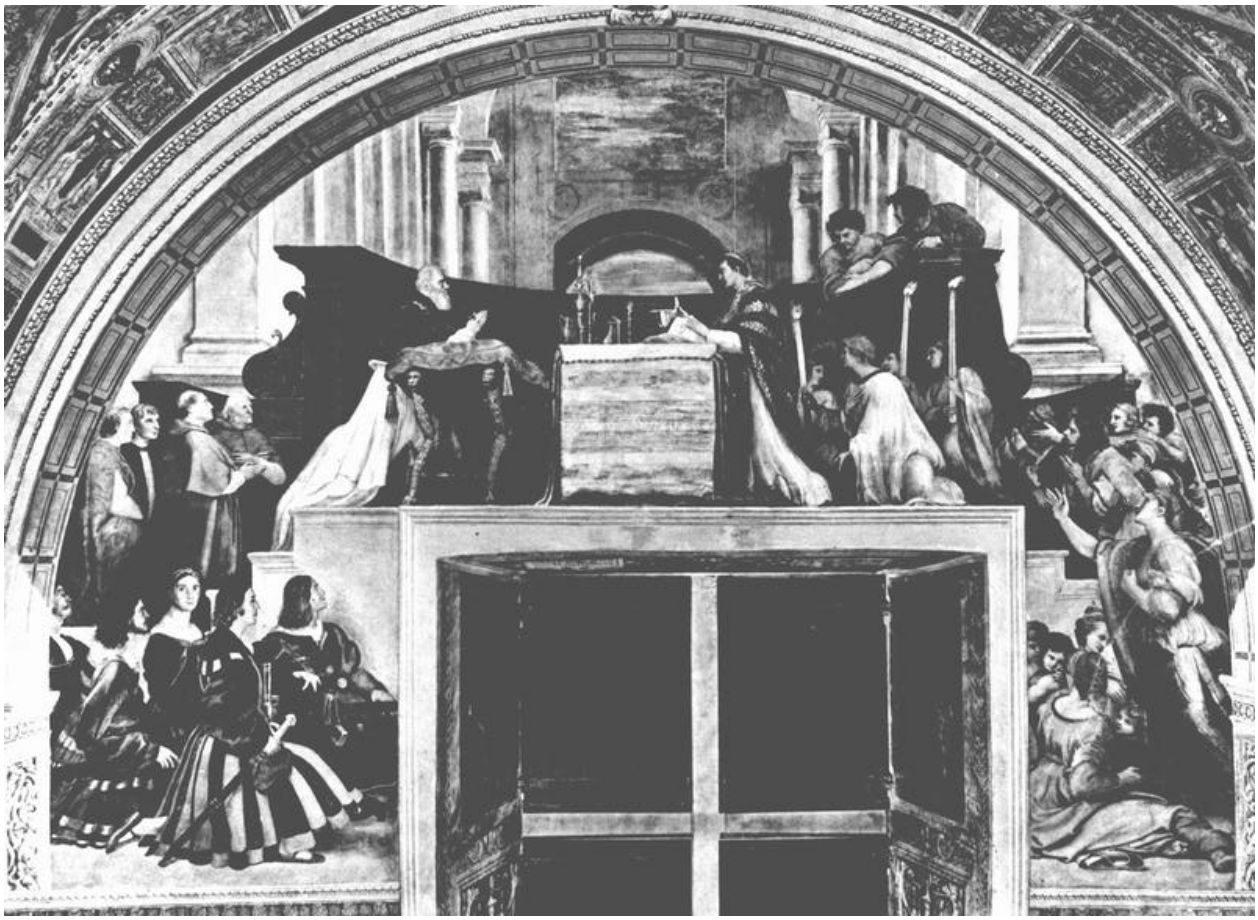
As a result of these disclosures, public hearings concerning biologic testing in the public domain were conducted in 1977 by the United States Senate Subcommittee on Health and Scientific Research. Of concern to the senators was the secrecy of the experiments, which involved a large population of involuntary and unwitting subjects. Senator Richard Schweiker chastised the United States Army for continuing the use of S. marcescens as a biologic marker despite the fact that as early as 1952, Army personnel had been aware of the Stanford outbreak; yet the organism continued to be used as a biologic marker until 1968. Under the administration of President Richard Nixon, biologic warfare was renounced by the United States in 1969, and production of such biologic agents was halted. Spokesman for the Army were in the uncomfortable position of having to defend decisions made by others 20 to 30 years previously. Testimony from expert witnesses in the academic community not only questioned whether any microorganism could ever be considered wholly harmless but also criticized the scientific merits of the aerosolization experiments, citing design flaws and the limited usefulness of any information obtained.

Subsequently, analysis has cast doubt on the part that these aerosolization experiments may have played in the causation of infections. The Center for Disease Control in Atlanta, Georgia, has reported that in 100 outbreaks caused by S. marcescens in the United States, none were caused by a strain of serratia with the same serotype and biotype as that used by the United States Army.

Table 1. Open-air Biologic Simulant Testing Using Serratia marcescens in the Public Domain

Location	Date of Test :
Washington, D.C.	Aug. 1949, Dec. 1949, March 1980
Hampton Roads, VA*	April 1959
San Francisco, CA*	Sept. 1950
Key West, FL	1952
Panama City, FL	March to May 1952
Hawaii, HI	Jan. to March 1968

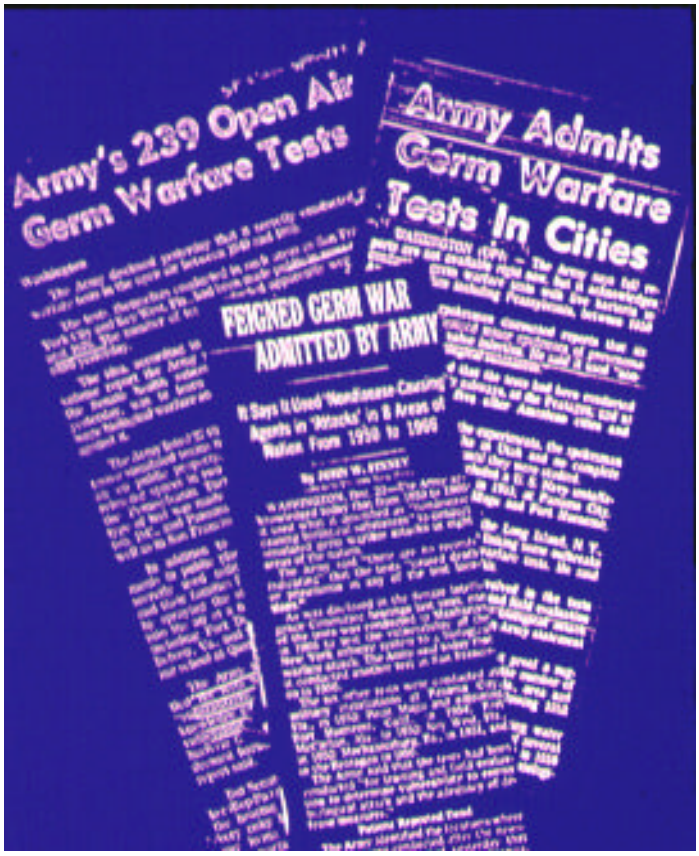
*Serratia released from ships at sea or at anchor.



Raphael's Mass of Bolsena at the Vatican

The Doubting Priest

Blood on Eucharist Bread



US Army experiments exposed in 1997 Congressional hearing

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