Germs, not putrid air, however, were proved to cause disease and, in 1893, oysters were named carriers of the disease in a typhoid outbreak in Connecticut. Thus, when the Baltimore Sewerage Commission in 1897 proposed a giant sewer dumping city wastes into Chesapeake Bay, the powerful oyster interests opposed and effectively blocked action. Baltimore was not the only culprit; smaller cities and towns always had dumped untreated sewage into Bay waters. Nonetheless, Baltimore's rapidly growing population made the problem more acute. Yet, in 1904, the oyster interests again prevailed in the General Assembly, and legislation prohibited the new sewerage commission from building any system "involving the discharge of sewage . . . into the Chesapeake Bay or any of its tributaries" (Chapter 349, Acts of 1904). Interpreting this restriction to mean untreated sewage, Baltimore resolved to have municipal sewage treatment. The City, formerly the only major city without sewage treatment, gained the most advanced, state-of-the-art system when its Back Bay plant opened in 1912.

Meanwhile, factors other than untreated sewage were recognized as polluting Chesapeake Bay. In 1910, the federal Public Health Service investigated pollution in both the Bay and the Potomac River. Truck farming and canneries had proliferated around the Bay, and the Public Health Service report agreed with the findings of the State Fisheries Commissioners that canning wastes harmed fisheries.

In that same year, the State Board of Health was reformed as the Department of Health, within which the Bureau of Sanitary Engineering was established (Chapter 560, Acts of 1910). The Bureau protected water purity, oversaw sewerage and water supply projects, and in time became concerned with industrial waste and air pollution. In 1914, the Department of Health was made responsible for "preserving the purity of the waters of the State" (Chapter 810, Acts of 1914). The Department's Bureau of Sanitary Engineering regulated public water supplies and sewerage systems and issued cease-and-desist orders to manufacturing or industrial establishments found polluting State waters with their wastes, if a threat to human health or a public nuisance. In 1918, two employees of the Department of Health developed a formula to chlorinate water thus ensuring a pure drinking water supply not only for Maryland, but ultimately worldwide. One of them — Abel Wolman —went on as sanitary engineer, and later consultant to more than fifty nations and helped bring safe drinking water to millions of people around the world.

Because concerns about water quality originated with fishery and oyster interests, in 1917 the Conservation Commission began to enforce abatement procedures for discharges which threatened fish and shellfish, or their "propagation, cultivation or conservation thereof, or to their safety as human food ..." (Chapter 14, Acts of 1917). Discharges from public sewage disposal plants were exempted, however, and the Commission prohibited from infringing upon the jurisdiction of the Department of Health.

The Conservation Commission sought cooperation from Maryland factory owners in treating their wastes to prevent industrial pollution. The Commission's 1917 annual report stated that no one would "wilfully persist in such an abuse" once they realized how untreated industrial wastes killed marine life. Lacking staff and facilities for scientific research or chemical analysis, the Commission's work to control pollution never received the same attention as did the condition of the oyster spat or the enforcement of game laws. Nonetheless, the Commission with the Department of Health began by examining pollution in the Curtis Bay area of Baltimore harbor. There, war-related industries had concentrated since 1914. Trade wastes exuded up to four million gallons per day from just one alcohol plant, whose attorneys in 1922 suggested that safeguarding Curtis Bay waters was impractical and impossible. They recommended that the area be designated an industrial zone exempt from water quality requirements. Despite the area's highly colored, thick and odoriferous waters, the Conservation Commission was unwilling to pinpoint Curtis Bay pollution as the cause of oyster decline in the Patapsco River and upper Chesapeake, blaming increased salinity and excess rainfall instead.

In the early 1920s, industrial pollution was overshadowed by oil pollution, a problem exceeding the enforcement capabilities of the Conservation Commission. Oil-burning ships pumped oil from their bilges in quiet waters of Chesapeake Bay and its harbors, devastating beaches, waterfowl, and oysters. Conditions were alleviated somewhat in 1924 when the federal Oil Pollution Act prohibited vessels from dumping oil in navigable waters. That act was only the second major federal law on water pollution; the first—the federal Rivers and Harbors Act—outlawed dumping debris in navigable waters in 1899.

The oyster faced a serious crisis in 1924. After a typhoid outbreak, eating raw oysters was outlawed in Illinois, and the U.S. Public Health Service began an investigation. In Maryland, oyster packing houses closed and soup kitchens opened on the Eastern Shore to feed the newly unemployed, even though Maryland's governor stated unequivocally that Maryland oysters never had caused a single case of typhoid. The Commission, reformed as the Conservation Department in 1922, strove to give the oyster a clean bill of health. This required regulation of oyster packing rather than water quality.

To control water pollution, the State Department of Health and the Conservation Department continued their cooperative work. The 1927 annual report of the Conservation Department optimistically claimed: