P. multocida. The subphysiological iron concentration of 19 μg per 100 ml was obtained by adding 15 g of $MgCO_3$ (to precipitate most of the iron) to 100 ml of the growth medium, stirring for 5 minutes, letting the solution stand for 15 minutes, centrifuging for 10 minutes at 2500*g*, and collecting the supernatant. This procedure was completed prior to sterilization of the growth medium. Another growth medium was prepared by adding 50 mg of deferoxamine mesylate (CIBA), an iron chelating agent, to 100 ml of the normally prepared growth medium. The deferoxamine mesylate was added to the growth medium just prior to inoculation with bacteria.

Prior to infection, the PI of eight rabbits averaged 247 μg of iron per 100 ml of plasma (68.1 percent saturation) in the morning and 275 μg per 100 ml (76.8 percent saturation) in the afternoon. After injection with bacteria, PI concentrations decreased to 118 μg per 100 ml (36.0 percent saturation) by 4 hours and to 66 μg per 100 ml (18.7 percent saturation) by 24 hours (Fig. 1). The TIBC did not change appreciably and remained at approximately 360 μg of iron per 100 ml of plasma.

Prior to injection with live bacteria, the rectal temperatures of the eight rabbits averaged 39.70° ± 0.17°C (standard error). Rectal temperature increased to 40.85°C ± 0.29°C by 4 hours after injection and was still somewhat elevated by 24 hours after injection (40.9° ± 0.30°C).

To determine whether an increase in temperature coupled with a reduction in iron concentration decreases the growth rate of *P. multocida*, we grew the bacteria in vitro at afebrile (39° and 40°C) and febrile (41°, 42°, and 43°C) temperatures at various concentrations of iron from subnormal (19 μg of iron per 100 ml) to normal concentrations encountered during infection (79 and 139 μg per 100 ml), to normal concentrations in uninfected rabbits (266 μg per 100 ml). In addition, we determined the effects of deferoxamine mesylate on these bacteria at various temperatures (Fig. 2).

The addition of deferoxamine mesylate to the growth medium slightly inhibited the growth of the bacteria at 39° and 40°C, severely attenuated the growth at 41°C, and completely prevented the growth at 42° and 43°C. The addition of this iron chelator did not reduce the concentration of iron in the medium but did reduce the availability of the iron to the growing bacteria.

These results indicate that in response to infection, PI decreases and body temperature rises; they also support the hypothesis that very small changes in temperature, corresponding to a moderate fever, coupled with a reduction in PI may be part of a coordinated host defense response. In vivo, the growth of many microorganisms is inhibited in large part by their inability to obtain adequate amounts of iron, because virtually all PI is bound to transferrin [see review in (*19*)]. The virulence of many pathogenic bacteria seems to be related to their ability to obtain adequate amounts of iron from the host's iron-binding proteins (*20*). As such, the increase in survival rate (*1-3*) in febrile organisms might be related, in part, to the synergistic effects of temperature and reduced iron on the growth of the pathogenic microorganisms.

If these results can be extrapolated to organisms pathogenic to human beings, then the use of drugs to reduce or attenuate moderate fevers during bacterial infections may limit to a certain extent the host defense response. It is also possible that the addition of excess iron to our diet (through fortified foods and minerals, for example) increases the growth potential of pathogenic bacteria and harms some individuals who already have adequate iron stores. In fact, these data along with those of Sword (*21*) and others (*9-11, 14*), raise the possibility that drugs such as deferoxamine mesylate or other iron chelators could have therapeutic value during certain bacterial infections.

MATTHEW J. KLUGER
BARBARA A. ROTHENBURG
Department of Physiology, University of Michigan Medical School, Ann Arbor 48109

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17. For the PI determinations, equal parts of plasma and trichloroacetic acid (1.22*M*) were mixed in polystyrene culture tubes, heated at 90°C for 15 minutes (to denature the protein molecules), and centrifuged for 10 minutes at 2500*g*. The supernatant was saved for testing. The samples for the TIBC (the potential amount of iron that the plasma transferrin molecules can bind) determinations were prepared as follows. Two milliliters of a solution containing 6 μg of iron per milliliter [derived from Iron Stock solution I [see (*16*)] was added to 1 ml of plasma, mixed for 30 seconds, and allowed to stand for 5 minutes with occasional mixing. $MgCO_3$ (380 mg) was then added to the sample (to precipitate the unbound iron), mixed for 15 minutes, and allowed to stand for 15 minutes. The sample was centrifuged at 2500*g* for 10 minutes and the supernatant was then used as in the PI sample preparation. Iron concentration was determined on an atomic absorption spectrophotometer (Varian AA-375). Four absorbance values were obtained per sample with each value being determined over a 3-second period. Sample concentrations were determined by comparison of absorbance values to a standard curve. The standards were prepared according to the method of Fernandez (*16*). The percentage saturation of transferrin was calculated as: (PI/TIBC) × 100.
18. The bacteria were incubated for 44 to 48 hours at 37°C on 10 percent sheep blood agar plates, suspended in saline, centrifuged, and resuspended in saline. One hundred milliliters of the growth medium, brain heart infusion (Difco), were inoculated with 2 ml of the bacterial suspension. The medium was then placed in a temperature-controlled shaking bath (Forma Scientific) set at 39°, 40°, 41°, 42°, or 43° ± 0.2°C. Samples were taken after the first 15 minutes and every hour thereafter. Estimates of bacterial growth were determined by turbidity (absorbance) on a spectrophotometer (Beckman DB) set at 700 nm.
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Mineral Salt: A Source of Costly Energy?

The report by Wick and Isaacs (*1*) on the energy that can be obtained from salt and brine deposits through osmotic conversion neglects some basic economic problems associated with these energy sources: the costs of mitigating the environmental impact, the costs of the physical plant and maintenance, and mining

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costs. When these factors are poorly defined, our ability to predict the price of electric power from a source low in available energy must be greatly diminished.

The osmotic energy conversion of salt or concentrated brine would produce enormous quantities of effluent. Using the data of Wick and Isaacs, I calculate that at 100 percent conversion efficiency 300 metric tons of salt must be processed through a membrane system and 6.81 acre-feet of brine rejected to produce the energy equivalent to that in a ton of petroleum (*2*). For a 1000-MW power plant, the rejected brine would amount to 15,000 acre-feet per day, an enormous volume to pass through membranes and a significant volume when one considers the environmental impact either on aquifers or on the marine environment. Loeb cited equipment costs comparable to those for thermal energy conversion but he did not include costs for pretreatment of saturated brine, environmental controls, or membrane maintenance (*3*).

The energy costs of mining salt place an additional debit on the net energy return. The minimum energy required to bring 1 ton of salt to the surface from 800 m (one-half the depth of the average salt dome) is 7.5 percent of the energy obtained at 100 percent conversion (*4*). This figure neglects costs associated with leasing, drilling, well casing, and maintenance. Perhaps the cost of mining salt is more accurately indicated by the present price of salt, $20.57 per ton (*5*) or $0.65 per kilowatt-hour, compared to fuel oil costs of $0.02 per kilowatt-hour (*6*).

Although salt domes and brines represent energy reserves larger than those of petroleum, because of their low available energy we can ill afford to pay unanticipated energy conversion costs. A thorough engineering analysis of salt mining, the conversion process, and brine disposal should be conducted so that this energy source may be seriously compared to other energy sources offering greater available energy and having less environmental impact.

W. GARY WILLIAMS
Clearwater Consultants, Inc.,
551 Boylston Street,
Boston, Massachusetts 02116

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3. It is assumed that rejected brine has a concentration of approximately 70 parts per thousand.
4. The minimum energy required to raise salt to the surface is the work required to pump salt water into a solution cavity against the greater hydrostatic pressure of saturated brine.
5. This price is f.o.b. the minehead, in Louisiana. This is a current price quoted by the Diamond Crystal Salt Company, St. Clair, Minn.
6. Utilities in the Boston area currently pay $12.75 per barrel (1 barrel = 159 liters) for residual fuel oil and generate 600 kWh per barrel consumed.

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Williams is quite properly impressed by the volumes of flow that occur in a large (1000-MW) power plant utilizing salinity gradient energy from concentrated sources, although his calculations appear to be high by an order of magnitude. Yet this flow (about 1000 acre-feet per day) is of the same order of magnitude as the flow of cooling water of a conventional or nuclear thermal power plant, and more than an order of magnitude less than the flow from a nominal hydroelectric or Ocean Thermal Energy Conversion plant of the same power rating. Williams erroneously assumes that this total flow must be made to pass through membranes and that it will require considerable preliminary treatment. Osmotic flow through membranes (for example, as in pressure-retarded osmosis) has, in our opinion, low probability for successful conversion of this energy in large-scale plants. In the process of inverse electrodialysis, only the ions pass through membranes and electric power is directly generated. The process of reverse vapor compression requires neither membranes nor extensive pretreatment of the fluids (*1*).

In principle, any reversible process of desalination can generate power in reverse (that is, salination). One of the most efficient desalination processes developed is vapor compression distillation. This process is conducted wholly through the vapor phase, and no membranes are involved. Generating power with the reverse process of vapor compression distillation has been explored in the laboratories of the Foundation for Ocean Research. The efficiencies of power extraction from brine versus freshwater have been of the order of 70 percent, with power densities of the order of 2.5 to 7.0 W per square meter of evaporator-condenser surface (*2*). Salinity gradient power extraction does not appear to be subject to fundamental efficiency limitations, such as Carnot efficiency for thermal plants, but can approach 100 percent for low rates of generation.

Williams is appropriately concerned with the environmental impact of effluent discharge. If salinity gradient power were to be generated at sites where mixing normally is taking place (for example, stream flow into brine lakes or seawater flow into coastal salt pans), the environmental disturbance of the effluent would be negligible.

However, as Williams points out, brine effluent from a large salt-dome, salinity-gradient power plant probably cannot be so readily disposed of. We have suggested the probably expensive approach of reinjection (*3*). Simpler solutions may be possible. Discharged into the outflow of the Mississippi, the brines from several plants would be a negligible addition to the salinity.

Our purpose in (*3*) was to point out the existence of a large source of power with an available energy density one or more orders of magnitude greater than many sources now being used or seriously contemplated (for example, wind, ocean currents, waves, tides, ocean thermal, and hydroelectric) (*4*). We join Williams in calling for a thorough engineering evaluation and also a scientific evaluation of salt and brine deposits as energy sources.

GERALD L. WICK
JOHN D. ISAACS
Institute of Marine Resources,
Scripps Institution of Oceanography,
University of California at San Diego,
La Jolla 92093

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13 November 1978