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23. We thank W. S. Broecker for calling our attention to Richardson's thesis (*3*) and for providing us with a copy. This research has been carried out under contract for the United Kingdom Department of the Environment as part of its radioactive management research program. The results will be used in the formulation of government policy but, at this stage, do not necessarily represent that policy.

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Sulfate and Nitrate Concentrations from a South Greenland Ice Core

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An ice core in south Greenland covering the period 1869 to 1984 was analyzed for oxygen isotopes and chloride, nitrate, and sulfate concentrations. The data show that the "excess" (nonsea-salt) sulfate concentration has tripled since approximately 1900 to 1910 and the nitrate concentration has doubled since approximately 1955. The increases may be attributable to the deposition of these chemical species from air masses carrying North American and Eurasian anthropogenic emissions.

ONE OF THE MAJOR PROBLEMS associated with determining the effects of fossil fuel burning and acid deposition through time has been the lack of a reliable historic database for comparison with recent precipitation chemistry. Although it is believed that the hydrogen ion, sulfate, and nitrate concentrations in precipitation in the Northern Hemisphere have increased in the last few decades, detailed, continuous, long-term records in which there has been consistency in the way the samples have been collected, handled, and analyzed are lacking (*1*). Snow and ice cores collected from glaciers provide an opportunity to determine the chemistry of previously deposited precipitation and hence allow the production of reliable historic databases for areas remote from local anthropogenic influences.

In 1984, an electromechanically drilled core (*2*) was recovered from a site (65.01°N, 44.87°W, 2615 m above sea level) 40 km southwest and up-ice from a previously drilled site (Dye 3) in south Greenland. The site is believed to be free of any local contamination produced by Dye 3 (*3, 4*) and is located directly downwind from seasonally directed air masses that emanate from North America and Eurasia. It is ideal for the recovery of ice core records in general (*5*). Earlier chemical studies at Dye 3 by Herron (*6*) and Neftel *et al.* (*7*) have demonstrated the value of recovering records of sulfate and nitrate from south Greenland. However, these studies were based on multiyear averages of data over the last two millennia (*6*) or annual values since 1895 (*7*). Our record displays a total of 748 samples, equivalent to 6.5 samples per year, analyzed for chloride, "excess" sulfate (nonsea salt), nitrate, and oxygen isotopes (Fig. 1), as well as sodium (*8*), for the period 1869 to 1984 from a site unaffected by local contamination and hence valuable as a measure of North American and Eurasian anthropogenic activity.

All materials that contacted the samples were extensively tested (*8*) to ensure that the core was collected and processed without contamination. We used a cleaned polycarbonate subcorer to remove the outer 40 to 50% of core to guard against contamination potentially introduced during drilling. Blanks for the subcoring technique and the sample containers were <1.0 μg kg^{-1} for chloride and nitrate, <2.0 μg kg^{-1} for sulfate, and <2.7 μg kg^{-1} for sodium. All laboratory sample handling and processing before analysis was conducted in a cold room (−20°C). In the anion analyses we used a Dionex model 2010 ion chromatograph with an AS-4 column and $0.0021M$ $NaHCO_3/0.0017M$ Na_2CO_3 eluent and a computer-driven autosampler. In the sodium analysis we used a stabilized-tempera-

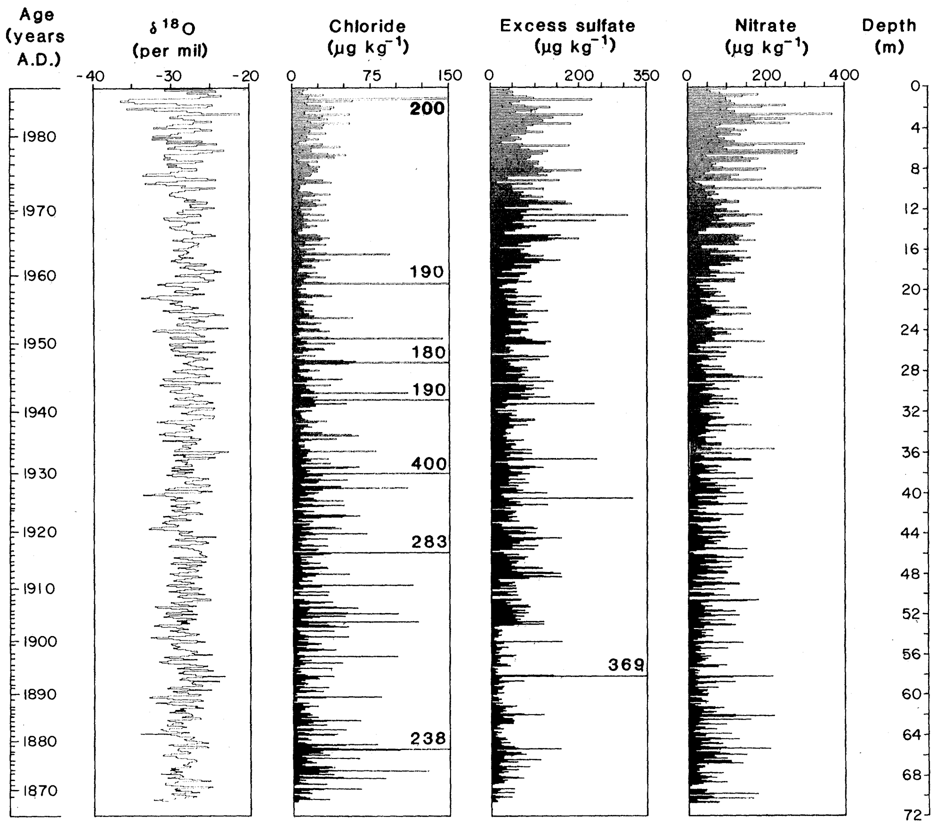

Fig. 1. Oxygen isotope, chloride, "excess" sulfate, and nitrate time series. Chloride and "excess" sulfate values that are off-scale appear as numbers. The time scale is compressed to accommodate annual layer compaction with depth.

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ture, platform-furnace atomic absorption spectrometer (Perkin-Elmer model 2280). We analyzed over 12% of the samples in duplicate, using two separately drawn aliquots; this procedure yielded precision values for chloride, nitrate, sulfate, and sodium of 3, 5, 3, and 10%, respectively. Oxygen isotope and total β-activity analyses were used to determine core chronology. In the oxygen isotope analyses we used gas-source mass spectrometry. A Canberra model 2404 alpha-beta-gamma counter was used to count the total β-activity of 132 250-ml samples that had been gravity-filtered through 47-cm Whatman SA-1 cation filters. Total β-activity measurements (*8*) from the upper 18 m of this core together with the oxygen isotope data from the core and the total β-activity records and oxygen isotope data from a core located 4 km to the northeast, analyzed by the University of Copenhagen, were used to assign core chronology.

According to linear regression analysis, the oxygen isotope record displays no significant trend with time, except that there is a slightly larger seasonal variation in the upper 10 m of the core that below this depth is dampened as a result of diffusion. The apparent absence of trend indicates that the area close to the drill site has not experienced any significant changes in annual average temperature throughout the period 1869 to 1984.

Chloride in the ice core has both marine and volcanic sources. Ratios of chloride to sodium (geometric average, 2.4; 1 σ range, 1.2 to 4.4) are relatively close to the value expected for seawater (≅1.8) except for several maxima, which are believed to be attributable to volcanically derived chloride (*6, 8, 9*). Except for seasonal variations in chloride (*10*), which are not easily interpreted in the sodium/chloride ratios because of variability in sodium produced by its combined marine and crustal sources, no significant trend is identifiable for the period 1869 to 1984 on the basis of linear regression analysis. Therefore, since most of the chloride has a marine origin, it may be inferred that transport distances from the ocean and drill-site elevation have remained stable over the period covered by the core.

If both temperature and ocean-to-drill site distances have remained fairly constant for the period 1869 to 1984, it is probable that the accumulation rate in the area has also remained constant (*11*). Therefore, climatically induced variations in the chemical species time series probably have a negligible effect on this record. In particular, chemical species with gaseous precursors such as sulfate and nitrate, whose concentrations are accumulation rate–dependent (*6*) can be interpreted directly, without accumulation rate adjustments.

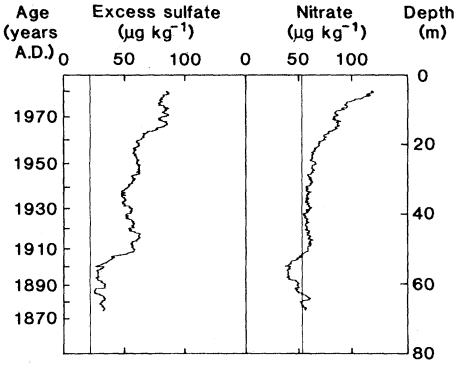

Fig. 2. Ten-year running means for "excess" sulfate and nitrate. Vertical lines at 22 μg kg^{-1} for "excess" sulfate and 55 μg kg^{-1} for nitrate represent "old" ice values based on values from Herron (*6*).

The sources of sulfate in Greenland precipitation are well documented, with contributions from sea salt, biogenic emissions, and volcanism (*9*) as well as anthropogenic activity (*6, 7, 12*). Although volcanic input occurs at random intervals in the record, the other sources display regular seasonal signals (*10*). The amount of sea salt–associated sulfate in the ice core is generally small (≅3 μg kg^{-1} in mean value). When the sea salt–associated sulfate is subtracted from the total sulfate, the result is "excess" sulfate. Biogenically produced sulfate is thought to be due primarily to the emission of gaseous sulfur compounds from both soils and marine waters (*6*). Recently, it was shown that the ocean can be a major source of gaseous sulfur to the atmosphere (*13*) and hence can contribute to the natural sulfate background in the ice core record.

Changes in trend in the ice core "excess" sulfate record can be separated into the following approximate groupings (Fig. 2): from 1870 to 1900, relatively constant; from 1900 to 1910, sharply increasing; from 1910 to 1940, relatively constant; from 1940 to 1960, generally increasing; from 1960 to 1968, sharply increasing; and from 1968 to 1984, relatively constant. Abrupt rises in "excess" sulfate such as the one between 1900 and 1910 probably represent volcanic input of sulfate (*6, 9, 14*). The mean "excess" sulfate value for 1870 to 1900 is 30 μg kg^{-1}, which is similar to the value (22 μg kg^{-1}) measured by Herron (*6*) in "old" ice (Fig. 2), and thus the value for 1870 to 1900 is probably very close to the natural background value. The difference between the two values may be due entirely to differences in the sampling interval used in the respective studies. The mean "excess" sulfate for 1968 to 1984 is 84 μg kg^{-1}.

Since 1870 the global anthropogenic annual emission of sulfur has increased by a factor of approximately 25, with the highest rate of increase between 1930 and 1940 (*15*). In North America, the present anthropogenic sulfur flux is thought to be ten times as high as the natural flux (*16*) and to be enriched 2 to 16 times relative to remote precipitation (*17*). Budgetary calculations for North America indicate that at least 25% of the anthropogenic sulfur emissions leave the region and move eastward (*16*). The work of Herron (*6*) and Neftel *et al.* (*7*) and the results presented here demonstrate that the sulfate deposition in south Greenland precipitation now is approximately three times what it was at the turn of the century. In addition, this work documents the estimated increase of global anthropogenic sulfur since 1940 (*15*). Thus, our data and those of others (*6, 7*) indicate that this anthropogenic sulfur of North American origin and that from Eurasia (*18*) are detectable as increased sulfate loading in south Greenland ice cores, despite the fact that fractionation processes dilute the record in remote areas.

The sources of nitrate to south Greenland precipitation are thought to include anthropogenic activities such as fossil fuel and biomass burning and unknown natural sources, primarily of biogenic origin (*6, 7*). Volcanic sources of nitrate are thought to be small contributors to this area (*6, 19*) although several nitrate maxima may have volcanic sources (*9*). It is unlikely that other sources of nitrate (*20*) are important in south Greenland. The south Greenland nitrate record displays a strong seasonal signal (*6, 10, 19*).

Changes in trend in the nitrate record of the ice core (Fig. 2) indicate a relative constancy in value from 1869 to 1955, followed by a period of general increase from 1955 to 1975, and an intensified increase from 1975 to 1984. The mean nitrate value for 1869 to 1955 is 55 μg kg^{-1}, which is the same as the value derived by Herron (*6*) for "old" ice. The mean value for 1975 to 1984 is 115 μg kg^{-1}, suggesting a twofold increase in nitrate since the late 1950's. The magnitude of this increase is in good agreement with earlier results in south Greenland (*6, 7*) and with emission records from North America (*21*).

In summary, this ice core record is derived from a site that is devoid of any locale-specific contamination, and it is the longest and most detailed record of anthropogenically introduced sulfate and nitrate yet available. The initial date for the increase in "excess" sulfate is approximately 1900 to 1910 with a second period of increase starting in approximately 1940; for nitrate the initial date of increase is approximately 1955. The increase in "excess" sulfate in our record (by a factor of 3) is very close to the estimated increase (by a factor of 2.5) determined from a calculation of the export of sulfate from North America eastward, according to emission and deposition modeling (*18*).

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11. This argument is substantiated by comparison of our core data with that for the University of Copenhagen core 4 km to the northeast. There are differences in the accumulation rate between the two sites only for the period 1966 to 1974, and these are believed to be due to the loss in our core of approximately 2 to 3 years of record within the lower density, more easily damaged section.
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Control of Cachectin (Tumor Necrosis Factor) Synthesis: Mechanisms of Endotoxin Resistance

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Cachectin (tumor necrosis factor) is a macrophage hormone strongly implicated in the pathogenesis of endotoxin-induced shock. The availability of a DNA probe complementary to the cachectin messenger RNA (mRNA), as well as a specific antibody capable of recognizing the cachectin gene product, has made it possible to analyze the regulation of cachectin gene expression under a variety of conditions. Thioglycollate-elicited peritoneal macrophages obtained from mice contain a pool of cachectin mRNA that is not expressed as protein. When the cells are stimulated with endotoxin, a large quantity of additional cachectin mRNA is produced, and immunoreactive cachectin is secreted. Macrophages from mice of the C3H/HeJ strain do not produce cachectin in response to endotoxin. A dual defect appears to prevent cachectin expression. First, a diminished quantity of cachectin mRNA is expressed in response to low concentrations of endotoxin. Second, a post-transcriptional defect prevents the production of cachectin protein. Macrophages from endotoxin-sensitive mice do not produce cachectin if they are first treated with dexamethasone, apparently for similar reasons. These findings give new insight into the nature of the C3H/HeJ mutation and suggest an important mechanism by which glucocorticoids may act to suppress inflammation.

CACHECTIN (*1*) IS A MACROPHAGE hormone produced in large quantities in response to endotoxin (*1–3*) or other stimuli simulating host invasion (*3*, *4*). When administered intravenously, cachectin binds to a wide variety of tissues via a specific high-affinity receptor (*1*). After binding, it acts to suppress the expression of several specific messenger RNA (mRNA) species (*5*), thus effecting widespread changes in cellular metabolism. In adipose tissue, cachectin causes complete suppression of the enzyme lipoprotein lipase, thereby preventing the uptake of exogenous triglyceride by fat cells and causing the paradoxical lipemia frequently associated with infection (*6*, *7*) or neoplastic disease (*8–10*).

We recently suggested, on the basis of NH_2-terminal sequence data and comparative bioactivity studies, that cachectin and tumor necrosis factor (TNF) are identical proteins (*11*). This identity has been confirmed by genetic sequence analysis (*12–14*) and serves to underscore the broad range of bioactivities attributable to the hormone. We also demonstrated that BALB/c mice passively immunized against cachectin become markedly resistant to endotoxin [lipopolysaccharide (LPS)] (*15*), and have noted (*16*) that animals treated with relatively small doses of cachectin develop metabolic acidosis and a potentially lethal state of shock. These observations suggest that cachectin plays a central role in the pathogenesis of endotoxin-induced shock.

Here we address the mechanism of cachectin induction by endotoxin in peritoneal macrophages. We also analyze the mechanism of endotoxin resistance, both in mice of the C3H/HeJ strain and in macrophages treated with dexamethasone in vitro.

Peritoneal macrophages from normal mice, or from animals primed with thioglycollate 5 days before they are killed, express low but detectable quantities of cachectin mRNA. It is not clear whether this low level of expression is the result of mRNA induction during isolation, or whether the mRNA is actually present in vivo. Immunoreactive cachectin, however, is not detectable in the medium of cultured macrophages prior to induction of the cells by endotoxin. Lysates prepared from noninduced cells also appear to lack the protein in measurable quantities. Once stimulated with endotoxin, peritoneal macrophages express greatly in-

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