

double helices have h values about 1 Å shorter than the single helices of chondroitin 6-sulfate (17). This shortening leads to more obviously grooved, helical structures (Fig. 2, c and d) that are apparently necessary to accommodate the second chain of a double helix. In the lower-humidity form regular double helices of hyaluronate pack 9.9 Å apart, which is essentially the same as their distance of closest approach in the high-humidity form. This distance is much closer than has been observed for chondroitin 6-sulfate or ι -carrageenane, where the lattice has to accommodate protruding sulfate groups.

The conformational flexibility of the extended single chains of chondroitin 6-sulfate is in marked contrast to the relatively rigid molecular conformations imposed by the double helical structures of hyaluronate and ι -carrageenane. The existence of double helices for both of these shows that sulfation or its absence is not a prerequisite for coaxial helices. Chemical differences between chondroitin sulfate and hyaluronate are amplified by their secondary structures, which presumably provide additional specificity for their biological functions.

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References and Notes

1. Films a few hundred micrometers thick are cast on Teflon blocks. Strips 0.5 by 0.2 cm are stretched under constant tension (about 3 g) at 80 to 90 percent relative humidity. The procedure is similar to that described in (15).
2. Chondroitin is a polydisaccharide in which a β -D-glucopyranuronic acid residue is linked 1 \rightarrow 3 to a 2-acetamido-2-deoxy- β -D-galactopyranose residue that is in turn linked 1 \rightarrow 4 to the next glucopyranuronic acid residue. In the 6-sulfate the site of esterification is the galactopyranose. Structural formulas are given in a review by H. Muir, *Amer. J. Med.* **47**, 673 (1969).
3. We have used chondroitin 6-sulfates extracted from ray cartilage (which are occasionally further sulfated at C2 or C3 of the glucopyranuronic acid) or from squid cartilage (which has some additional sulfation at C4 of the galactopyranose). We have also used chondroitin 6-sulfate from shark cartilage and skin, additionally sulfated at C2 or C3 of the glucopyranuronic acid (Sigma Chemical Co., St. Louis, and Seikagaku Kogyo Co., Tokyo).

4. Figure 1A corresponds to threefold helical molecules because there are meridional reflections only on layer lines 3, 6, and 9; Fig. 1B corresponds to eightfold helical molecules since there are meridional reflections only on layer lines 8, 16, and 24.
5. The threefold helices pack in a trigonal lattice ($a = 14.3$ Å and $c = 28.7$ Å), and the eightfold helices in a tetragonal lattice ($a = 13.8$ Å and $c = 78.2$ Å). Definitions of these terms are given by K. C. Holmes and D. M. Blow, in *Methods of Biochemical Analysis*, D. Glick, Ed. (Interscience, New York, 1965), vol. 13, p. 147. E. D. T. Atkins, R. Ganssen, D. H. Isaac, V. Nandanwar, J. K. Sheehan [*J. Polym. Sci. Part B* **10**, 863 (1972)] have just reported a threefold chondroitin 6-sulfate helix with $c = 28.5$ Å. Although they have tentatively interpreted their diffraction pattern as showing orthorhombic symmetry, we suspect that their structure is essentially the same as our trigonal form.
6. M. B. Mathews, *Biochem. J.* **125**, 37 (1971).
7. Conformation angles corresponding to the centers of "fully allowed" regions were determined by the method of D. A. Rees [*J. Chem. Soc. B* (1969), p. 217], but by using as fixed stereochemical parameters the averaged bond lengths, bond angles, and (C1 chair) pyranose geometry in (8). Model conformation angles were allowed to deviate minimally from these idealized values to attain the observed values of h and θ as described in (8).
8. S. Arnott and W. E. Scott, *J. Chem. Soc. Perkin Trans. II* (1972), p. 324.
9. Left-handed chains are shown. We have no good stereochemical reasons for preferring left-handed rather than right-handed helices. A preference must await detailed structure refinement involving the intensities of the x-ray diffraction data. The general features that we wish to discuss here are effectively the same for helices of either hand.
10. The unacceptably short distance (2.5 Å) is between the ring oxygen (O5) of the galactopyranose residue and C4 of the glucopyranuronic acid residue. This distance cannot be increased merely by adjusting conformation

angles at the glycosidic bridges but will require some small change in the shape assumed for the pyranose rings.

11. N. S. Anderson, J. W. Campbell, M. M. Harding, D. A. Rees, J. W. B. Samuel, *J. Mol. Biol.* **45**, 85 (1969); S. Arnott, W. E. Scott, D. A. Rees, C. G. A. McNab, in preparation
12. A. G. Ogston, in *Chemistry and Molecular Biology of the Intercellular Matrix*, E. A. Balazs, Ed. (Academic Press, New York, 1970), pp. 1231–1240; M. B. Mathews, in *The Connective Tissue*, B. M. Wagner and D. E. Smith, Eds. (Williams & Wilkins, Baltimore, 1967), pp. 304–329.
13. In hyaluronate, 2-acetamido-2-deoxy- β -D-glucopyranose replaces the galactopyranose of chondroitin. It contains no sulfate groups. We have used sodium hyaluronate of high molecular weight (weight average, 1.3×10^6) extracted from human umbilical cord.
14. I. C. M. Dea, R. Moorhouse, D. A. Rees, S. Arnott, J. M. Guss, E. A. Balazs, *Science* **179**, 560 (1973).
15. E. D. T. Atkins and J. K. Sheehan, *ibid.*, p. 562.
16. This lower-humidity form gives a diffraction pattern very similar to that of the higher-humidity form (14). However, the tetragonal molecular packing ($a = 9.9$ Å and $c = 33.9$ Å) and the absence of meridional reflections on layer lines 2 and 6 indicate a regular fourfold helix. The higher-humidity form contains a perturbed version of this fourfold helix packed in an orthorhombic lattice ($a = 9.8$ Å, $b = 11.4$ Å, and $c = 33.7$ Å).
17. The double helices of hyaluronate can be destroyed by more extensive treatments; the result is molecular helices with h values in the higher range (9.3 to 9.5 Å), which have been interpreted as being single helices (15).
18. Supported by NSF grants GB-18835 and GB-35965 to S.A.; by grants from the Arthritis Foundation (to J.M.G.) and the Jane Coffin Childs Memorial Fund for Medical Research (to D.W.L.H.); and by PHS grants AM-05996 and HD-04583 to M.B.M.

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Ferromagnetic Contamination in the Lungs and Other Organs of the Human Body

Abstract. *Contaminating particles which are ferromagnetic have been found in the human body. Their distribution was measured by applying an external magnetic field to the torso for a short time, and then, in a shielded room, mapping the steady magnetic field around the torso due to the magnetized particles. Maps of subjects show various distributions, including particles in the stomach from food cans and in the lungs from arc welding. The fields from these two sources are strong enough to be detected with a flux-gate magnetometer, without the need for a shielded room. This simplicity of detection of larger amounts of ferromagnetic contamination suggests that this method may be used in two applications: in detecting the presence of large amounts of asbestos (ferromagnetic and harmful) in the lungs of asbestos workers, and in tests of the condition of the lung where FE_3O_4 dust (ferromagnetic and harmless) would be used as an inhaled tracer material.*

In recent years my colleagues and I have been investigating the steady (1) magnetic fields around the torsos of both humans and dogs produced by natural, internal direct current (d-c). Fields from d-c, although very weak, have been of interest because it has been believed that such fields can be a measure of heart injury (2). In mapping these fields around the torso I noticed that often there was another, steady field that was not due to internal d-c; instead, investigation showed that

this field was produced by ferromagnetic particles in the lungs, stomach, and other organs. These particles entered the body through food and air. This other steady field, therefore, was the remanent field of these particles, magnetized by the earth's field and other sources. Since these particles are foreign to the body and also interfere with the magnetic measurement of internal d-c, they have been named ferromagnetic contamination (FC). It was then suggested (3) that magnetic measure-

ment of FC in the human lung may be medically useful. As a result, in order to assess the range of normal and abnormal FC, I mapped the steady fields over the torsos of some 30 subjects, chosen both at random and for special FC. In this report I explain the measuring technique, briefly describe some of FC phenomena revealed by the mapping, and suggest two clinical applications of FC.

The main problem in measuring magnetic fields produced by the human body, either fluctuating or steady, is the magnetic background. For example, the magnetic pulsations from the human heart, which are about 10^{-6} gauss at maximum, are much weaker than the background fluctuations and are most simply measured in a magnetically shielded room which reduces the background fluctuations to far less than 10^{-6} gauss. The M.I.T. shielded room and SQUID detector (4), which have been used to measure fluctuating fields from the heart, brain, and muscle (5), have also been used for the steady-field measurements described here. However, in contrast to the measurements of the body's fluctuating fields which require the background fluctuations to be reduced below the level of these fields, steady-field measurements can be made in a steady background much higher than the steady fields. Consequently, for the measurements presented here, the steady-field background in the room was allowed to be $\sim 1 \times 10^{-4}$ gauss, much higher than the body's steady fields.

The technique I used consists of making a sequence of several magnetic maps, usually three, of the front of each subject's torso. The quantity mapped is the component of the steady magnetic vector that is normal to the skin, called B_n , measured about 3 cm from the skin. The first map is made after a 60-hz magnetic tape eraser (6) has been slowly wiped over the torso; this map is due to d-c and to particles which cannot be completely demagnetized (7). Next, another map is made after a steady magnetic field has been applied in a direction approximately normal to the skin, and then removed; this second map is due to d-c plus the field of the magnetized particles. Finally, by subtracting the first map from the second, a new map is produced which is due only to the magnetized particles. The quantity B_n at any point on this map is a function of the amount of ferromagnetic material behind that point, provided that B_n has a "positive"

polarity. As an example, consider one particle only, magnetized in a field normal to the skin of the chest. Leaving the chest side of the particle, a line of force would pass through the skin of the chest normally, eventually bend over, return through the skin some distance away, and bend over again to enter the back side of the particle. Hence this particle produces two polarities of B_n on the torso front: the polarity on leaving the skin, here defined as positive, and the negative polarity of the displaced return path. Only the positive B_n 's locate underlying material; negative B_n 's contain secondary information.

In order to accumulate the data for a map, a grid (5 by 5 cm) is marked on the front of the torso. Then, with the arrangement shown in Fig. 1, the following measurement is made at each grid point: the subject stands away

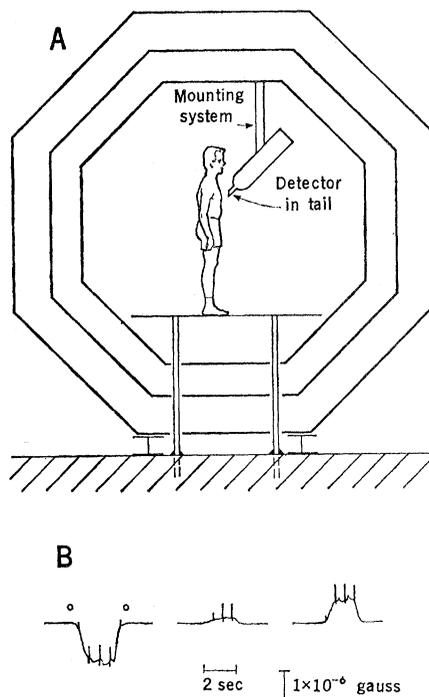


Fig. 1. (A) Arrangement for recording magnetic maps in the shielded room. The detector responds to the horizontal component of the magnetic vector, normal to the skin. The subject's clothing must be free of magnetic material, such as metal zippers, snaps, and shoe nails. (B) Three typical detector outputs from one subject. The shift in each is B_n . The first, showing a negative B_n , is from a location on the abdomen somewhat displaced from the stomach, after the subject had eaten this canned food, as displayed in lower Fig. 2A. The next two outputs, with positive B_n , are from a stomach location, before and after the subject had eaten this canned food. The torso was magnetized in all three cases. The bandwidth (0 to 30 hz) allowed the heart's pulsating field to be seen on each trace.

from the detector, then moves forward (first dot in Fig. 1B) and stands for a few seconds with the appropriate grid point close to the detector as in Fig. 1A, and then moves back again (second dot in Fig. 1B). The shift of the detector output is B_n at that grid point, which is finally displayed as a square on a sketch of the torso.

Representative maps of three subjects are shown in Fig. 2. The subjects fell into three groups. The first group consists of those who showed almost no FC in the lungs but a moderate amount in the abdomen, as in upper Fig. 2A. Most subjects tested were in this group, which I therefore call the normal group. The second group consists of those who had voluntarily ingested some FC for these studies, either in food or as an inhaled dust. An example is shown in lower Fig. 2A of a subject who ate some canned green beans; this example illustrates the source of much of the FC in the gastrointestinal tract. Most food cans are made from a ferromagnetic alloy, and microscopic particles are deposited into the canned food when the top is opened. The dust which was inhaled consisted of a small, controlled amount of magnetite (Fe_3O_4) particles, which are harmless but strongly ferromagnetic. The purpose was to evaluate the use of magnetite as a diagnostic tracer in the lung. Some results of the inhalation tests are presented below.

Before discussing the third group, the two maps of Fig. 2B, which are not produced by FC, are interjected here. They illustrate two common events, due to d-c, which can contribute to the map of the erased state. Upper Fig. 2B shows a pattern often encountered from currents in the abdominal region, of unknown origin. Lower Fig. 2B shows the typical pattern developed by most people after drinking cold water. This is the largest type of d-c event so far encountered, at times producing a steady field of $> 20 \times 10^{-7}$ gauss. The source of this reflex current is also not known.

The third group consists of those whose lungs had accumulated a significant amount of FC as a result of their occupations, such as the welder in Fig. 2C. Upper Fig. 2C shows no abdominal currents in the erased state, which is uncommon; there is a small negative field at the chest which is due to erasing, in this case, outside the shielded room in the earth's field, which gave a small "set" to the abundant FC in his lungs. This FC is easily seen in lower

Fig. 2C. The subject in this group with the most FC, about five times as much as the welder, had worked for many years at processing asbestos.

The coarseness of the spatial resolution of the maps of Fig. 2 is partly due to the magnetization method. The subjects were magnetized by a 500-gauss field, approximately normal to the torso front, from an available "pancake" coil, against which their backs were placed. With this magnetization, lower Fig. 2A and lower Fig. 2C show that the lungs and stomach can be roughly outlined. Better resolution is possible by using a more advanced scheme such as a uniform magnetizing field, and mapping

in two orthogonal directions, and by using a computer technique to sort out the information contained in the return paths.

In estimating the quantity of FC which produces a particular B_n , it was assumed that the FC is pure magnetite (8); magnetite and magnetically similar maghemite ($\gamma\text{Fe}_2\text{O}_3$) are the major ferromagnetic components in industrial dust, occurring either pure or in combination with magnetically inert material, as in asbestos (9). For the lungs, an integration was performed, yielding $\rho = 2 \times 10^{-2} B_n$, where ρ is the magnetite density in micrograms per cubic centimeter of lung in the region behind

a solid square, and B_n is in units of 10^{-7} gauss. In lower Fig. 2C, therefore, the region of lung behind D29 contains $0.6 \mu\text{g}$ of magnetite or maghemite per cubic centimeter of lung. The lowest density which can readily be determined by this method is based on a field of 0.5×10^{-7} gauss; this is the lowest B_n which is measurable without special care and yields $0.01 \mu\text{g}$ per cubic centimeter of magnetite or maghemite as the lowest density. In distributions more compact than those found in the lung, such as those found in the stomach, it was assumed that the FC is concentrated at a point, which yields, for the mass in micrograms:

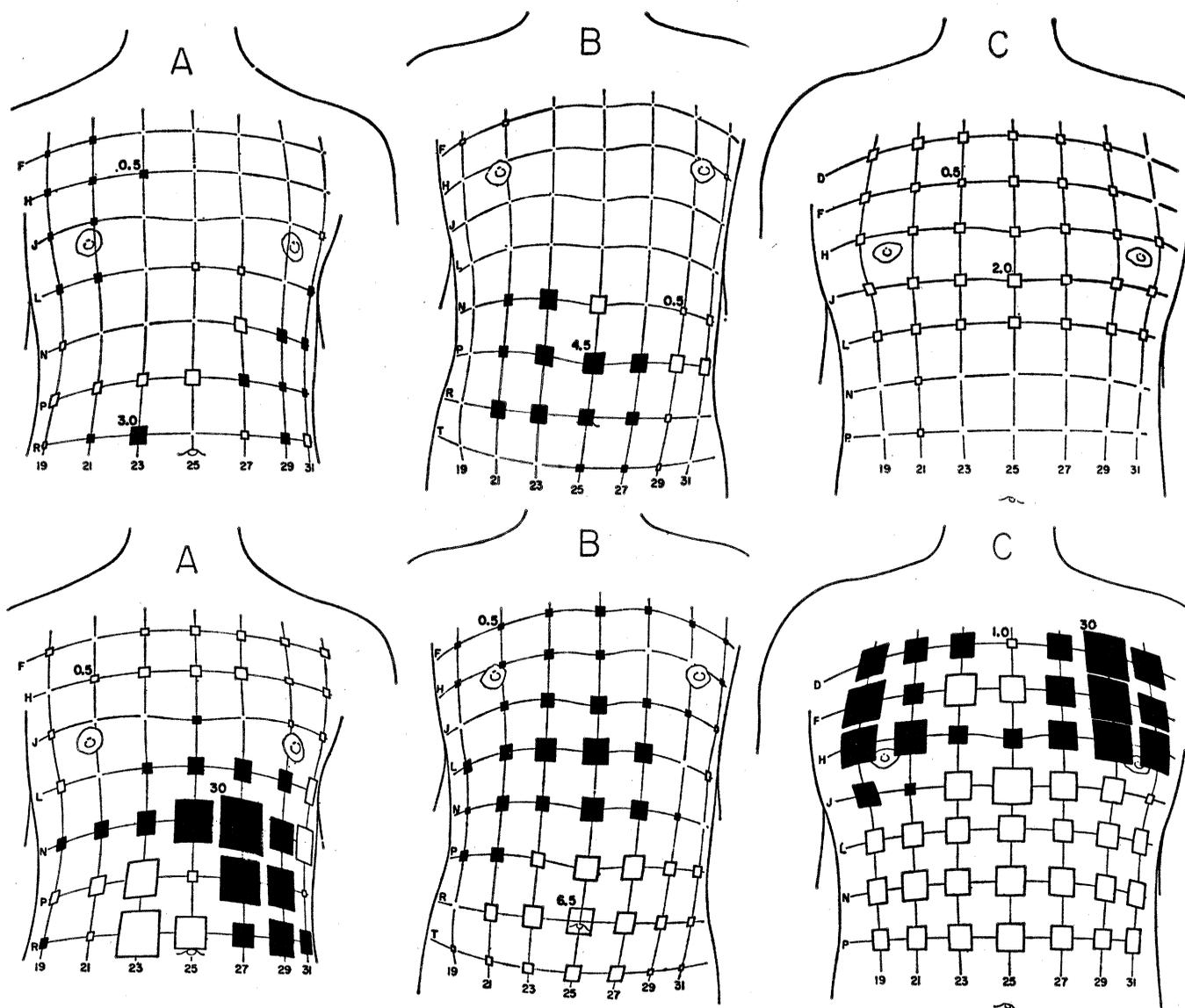


Fig. 2. Magnetic maps of three subjects. The grid junction L25 is always at the xiphoid. The areas of the squares are proportional to B_n , the normal magnetic component. Solid squares are positive and indicate underlying FC; open squares are negative and of secondary interest. The two numbers marked on each map are the largest and smallest (nonzero) B_n values on each map, in units of 10^{-7} gauss. (A, upper) Map due to the magnetized minus the erased state in a young man, showing a normal distribution of FC; (A, lower) map due to the magnetized state, recorded 10 minutes after the subject had eaten several forkfuls of canned green beans, minus (A, upper), showing the particles from the can in the stomach. (B, upper) Map of an erased state of a man in his 40's; (B, lower) map due to the erased state, recorded 10 minutes after the man had drunk cold water, minus (B, upper), showing the typical pattern produced by d-c from the "cold-water effect." (C, upper) Map of the erased state of an arc welder; (C, lower) map due to magnetized minus the erased state, which shows the accumulation of FC in his lungs.

$m = 10^{-2} d^3 B_n$, where d is the distance to the detector in centimeters. Therefore, in lower Fig. 2A, by assuming $d = 6$ cm, N27 indicates that there are a total of about 60 μg of can particles in the stomach (8).

Fields larger than about 20×10^{-7} gauss, as in lower Fig. 2A and lower Fig. 2C, can be detected with the simple and relatively inexpensive flux-gate magnetometer (10), in an urban environment, without the need for a shielded room. Because of this, two applications of this simple technique for the measurement of FC are suggested.

The first involves the asbestos worker. This subject in my measurements had been processing chrysotile asbestos (9) at a Quebec mine. His map showed $B_n \approx 150 \times 10^{-7}$ gauss at the lungs, but his chest x-ray was normal. This implies that a magnetic measurement can be a more sensitive indicator of FC actually present in the lungs, including asbestos, than an x-ray. (The arc welder of Fig. 2C also had a normal x-ray.) Therefore, if the ratio of magnetite to asbestos is known, flux-gate measurements may be useful in a mine area to monitor the accumulated asbestos in miners' lungs, in order to avoid the harmful effects of extreme accumulation (11). To check the simplicity of this technique, the magnetic field of the subject was measured outside the shielded room with a flux-gate magnetometer, and indeed the lung field was easily seen, well above the noise. The asbestos density, estimated from a field of 150×10^{-7} gauss (8), is 75 μg per cubic centimeter of lung.

The second application is the use of magnetite inhalation as a harmless tracer in determining rates of lung clearance and other processes. In the past, radioactively tagged (nonmagnetic) $\alpha\text{Fe}_2\text{O}_3$ dust has been used to measure lung clearance rates in humans (12), which gave knowledge of how the lung cleansed itself of fine dust. The magnetite inhalation tests presented here yield maps which resemble that of the welder in lower Fig. 2C, with lung fields of about 25×10^{-7} gauss; with the inhalation of a larger amount of magnetite, these fields would have been readily measurable with the flux-gate magnetometer outside the shielded room. The inhaled magnetite particles, as well as any FC in the lungs, show an interesting new phenomenon which is seen when a sequence of maps of a subject is recorded during the first few hours after a magnetization. The phe-

nomenon consists of the continuous decrease of all B_n 's, which drop by as much as a factor of 6 during the first hour; the decrease is most probably due to continuous rotations of the particles by some viable process in the lungs. The resulting relaxation curve is reproducible for each subject but varies from subject to subject; hence, this curve presumably contains information on both the particles and the condition of the lung. These results suggest that magnetite inhalation offers a new and useful probe of the lung.

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References and Notes

1. In the terminology used here, if a magnetic field is changing with frequencies slower than 0.1 Hz, it is called steady and is produced by either d-c or stationary ferromagnetic material; if it is changing faster than 0.1 Hz, it is called fluctuating and is produced by alternating current.
2. D. Cohen, J. C. Norman, F. Molokhia, W. Hood, Jr., *Science* **172**, 1329 (1971).
3. Suggestions were made by various associates, especially Prof. E. Rosenberg and A. Sandoval.
4. SQUID (superconducting quantum interference device) refers to a class of magnetic detector which is based on the Josephson effect, is extremely sensitive, and responds to d-c. The particular form I use was developed by Dr. J. Zimmerman and has been described in J. E. Zimmerman, P. Thieme, J. T. Harding [*J. Appl. Phys.* **41**, 1572 (1970)] and in D. Cohen, E. A. Edelsack, J. E. Zimmerman [*Appl. Phys. Lett.* **16**, 278 (1970)].
5. D. Cohen and D. McCaughan, *Amer. J. Cardiol.* **29**, 678 (1972); D. Cohen, *Science* **175**, 664 (1972); — and E. Givler, *Appl. Phys. Lett.* **21**, 114 (1972).
6. There are various tape erasers which are available commercially and are light enough to be held in one hand. The unit I use, a Robbins model TM-100, produces an amplitude of about 1000 gauss at a distance of 3 cm when powered by 208 volts.
7. Some magnetically hard particles, even though magnetized by the earth's field of about 0.5 gauss, cannot be demagnetized with the eraser I used. The demagnetization of ferromagnetic particles is discussed by T. Nagata in *Rock Magnetism* (Maruzen, Tokyo, 1961), p. 156.
8. The remanent magnetic moment of magnetite dust, after magnetization at 500 gauss, is about 6 electromagnetic unit/g. In the gastrointestinal tract, FC from cans is estimated to have ≤ 12 electromagnetic unit/g, similar to that of magnetite.
9. The fibers of chrysotile, which constitute 95 percent of the world's asbestos supply, occur with adhered magnetite particles which give asbestos its ferromagnetism and are difficult to remove in milling and refining. It is here assumed that the ratio by weight of magnetite to asbestos is 0.04, although it is higher before milling and lower after refining.
10. Flux-gate magnetometers have an equivalent input noise of $\leq 5 \times 10^{-7}$ gauss, root-mean-square, in a bandwidth of 0 to 1 Hz. Urban magnetic noise can usually be canceled out by the use of a differential input, such as with Automation Industry's MF-5000, used here for the tests with the asbestos worker.
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12. R. Albert, M. Lippmann, J. Spiegelman, A. Liuzzi, N. Nelson, *Arch. Environ. Health* **14**, 10 (1967).
13. The Francis Bitter National Magnet Laboratory is supported by the National Science Foundation. The author is an Established Investigator of the American Heart Association. This research was supported by grants from the American Heart Association (70-734), the National Science Foundation/RANN (GB-28136 and contract C670-2), and the National Institutes of Health (HE 13777-01). I thank Dr. G. Gibbs, Dr. R. Murphy, Mrs. A. Mackler, Dr. A. Langer, and Prof. I. Selikoff for supplying asbestos information and samples, Prof. H. Hardy for comments about the lung tests, and E. Givler for his low-field engineering, and the many other people who have given help and encouragement.

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Iguanid Lizard from the Upper Cretaceous of Brazil

Abstract. *Pristiguana brasiliensis*, new genus and species, from the Upper Cretaceous Baurú Formation of Brazil, is the oldest fossil referable to the living lizard family Iguanidae. It resembles living primitive South American iguanids in some features, but also shows similarity to members of the related family Teiidae. Iguanid fossils do not appear in North America until the early Eocene, probably by waif dispersal from South America during the late Paleocene or early Eocene. A southern continental (Gondwanan) origin of iguanids is more plausible than the northern one often suggested.

The lizard family Iguanidae is a primitive group distributed today in South America, Central America, and southwestern North America; two genera also occur on Madagascar and one on the Fiji and Tonga islands. The few fossils correctly referable to the family are currently being studied (1). Most of these fossils are North American forms that do not antedate the early Eocene (2, 3), a situation unusual in view of the present extensive Neotropical radiation and generic diversity among iguanids (at least 55 Recent genera are currently

recognized). Fossil iguanids occur in the Paleocene of Brazil (1, 4), but the specimen described here is of particular interest because it is the first Mesozoic record of the Iguanidae and the earliest record of the family.

Class Reptilia
Order Lacertilia
Family Iguanidae
Pristiguana brasiliensis
n. gen., n. sp.

Holotype: Divisão de Geologia e Mineralogia (DGM) No. 552, portion of a disarticulated skeleton of one individual,