perature a crossover to diamagnetism. The samples containing Sr^{2+} actually have yielded a higher onset temperature than those containing Ba^{2+} and Ca^{2+}. Furthermore, the diamagnetic susceptibility is about three times as large as for the barium samples. As the ionic radius of Sr^{2+} nearly matches the one of La^{3+}, it is clear that the size effect does not cause the occurrence of superconductivity. On the contrary, it is rather adverse, as the data on Ba^{2+} and Ca^{2+} indicate.

The highest T_c for each of the dopant-ions investigated occurs for those concentrations where, at room temperature, the La_2CuO_{4-y} structure is close to the orthorhombic-tetragonal structural phase transition (SPT) (*5*). Thus, this SPT may be related to the substantial electron-phonon interaction enhanced by the substitution. The alkaline earth–substitution of lanthanum is clearly important, and quite likely creates Cu^{3+} ions with two orbitals transforming as orbitals of the cubic e_g group which are half-filled and have a singlet ground state. Therefore, the absence of the third electron in the e_g states, which introduces a Jahn-Teller hole near the Fermi energy, probably plays an important role for the T_c enhancement as investigated theoretically (*16*). Referring to the theory of Höck *et al.* (*11*), one creates Jahn-Teller polaron holes by the doping. However, we cannot yet exclude an enhanced oxygen-vacancy content in the samples on alkaline earth–substitution to preserve charge neutrality. As the concentration of vacancies is finite, the role of pairs of Cu^{2+} and oxygen vacancies in the lattice needs to be investigated (*17*).

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Avascular Necrosis: Occurrence in Diving Cretaceous Mosasaurs

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A study of vertebrae of extinct giant marine lizards showed the presence of avascular necrosis in two of the three most common genera of these mosasaurs, *Platecarpus* and *Tylosaurus*. This bone disease was invariably present (involving 5 to 66% of vertebrae) in these genera, but absent in a third genus *Clidastes*. Differential occurrence of avascular necrosis may be related to decompression syndrome, suggesting different habitat and diving habits of the respective genera.

THE BONE PATHOLOGY, AVASCULAR necrosis, was found to be common in the skeletons of extinct giant marine lizards, the mosasaurs. The phenomenon was identified by its pathognomonic radiologic appearance (*1–3*), that of a linear region of radiolucency. This focal avascular necrosis (Fig. 1A) is quite different from the regional vascular changes resulting in tail loss in iguanids and the hoof and distal extremity loss occurring in grazing animals, secondary to ergotism. Whereas bone necrosis may occur in the latter circumstances, it is quite different from the linear necrotic pattern herein described in mosasaur vertebrae, where it is identical to the phenomenon known as avascular necrosis in man. Ischemic necrosis of vertebrae, presenting with an intravertebral radiolucent cleft is rare. All reported human cases that we have identified appear to manifest vertebral collapse, in addition to the intravertebral radiolucent cleft. Resnick considered this radiolucent cleft sign "virtually pathognomonic of bone necrosis" (*1*) as did Maldague (*2*). The vertebrae involved in man typically have included the tenth thoracic through the third lumbar, generally as an isolated phenomenon (limited to one vertebrae). Spinal involvement in avascular necrosis has thus been diagnosed by its radiologic appearance.

During study of a mosasaur vertebra with infectious spondylitis, we selected what appeared to be a normal vertebra for sectioning in order to characterize normal vertebral anatomy, and found a linear region of loss of tissue definition. The similarity of radiographs of this vertebra to those of vertebral bodies with avascular necrosis occasionally observed in man led to characterization of the nature of the bony change and a survey of the frequency of the pathology in caudal vertebrae in the University of Kansas Vertebrate Paleontology mosasaur collection.

Vertebral material in the collection belongs mostly to three genera of mosasaurs, *Platecarpus, Tylosaurus*, and *Clidastes*. Avascular necrosis was identifiable in all specimens of *Platecarpus* and *Tylosaurus* in the collection and in none of *Clidastes* (Table 1). The percentage of vertebrae involved in a given individual (Table 1) was greater for *Platecarpus* (mean ± SEM, 25.2 ± 5.5) than for *Tylosaurus* (9.1 ± 1.2) ($t = 2.36$, $P < 0.03$).

The vertebrae had no external evidence of vertebral collapse. Their size was the same as that of unaffected vertebrae. Radiologic examination revealed a radiolucent cleft (Fig. 1A). The cut surface revealed a linear area of loss of bone definition (Fig. 1B), confirmed on scanning electron microscopy. This can be distinguished from vascular channels by absence of sharply defined, radiodense margins. The relative localization of this abnormal zone within a given vertebrae corresponds to localization of vertebral avascular necrosis in man (*4, 5*) which in man represents a watershed region of vascular supply (*6*). Localization of perforating vertebral vessels in *Platecarpus* (Fig. 1C) is consistent with their location in man. Figure 1D shows on transverse section the vascular supply in *Platecarpus*, which is similar to that reported in man (*6*). The fossil occurrences differ from reported cases of avascular necrosis in man only in that vertebral collapse does not occur in the mosasaur specimens (*4*), and osteoporosis, reported in 65% of human cases (*7, 8*), was not identifiable in the mosasaur specimens. The relatively uniform width of the clefts would not be compatible with a diagnosis of metastatic carcinoma. Absence of irregular finger-like radiolucen-

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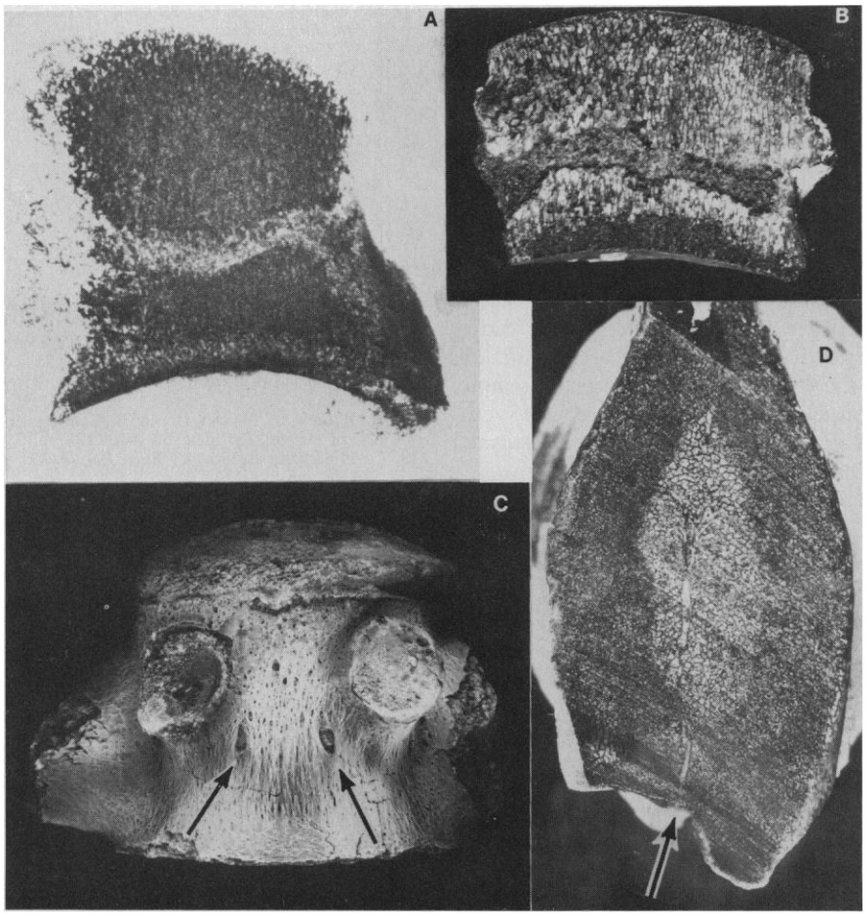

Fig. 1. *Platecarpus* cf. *coryphaeus* vertebrae. (**A**) Xeroradiography lateral projection of a caudal vertebra; pericentral transverse zone of radiolucency present. (**B**) Sagittal section of caudal vertebrae; pericentral area with transverse zone showing loss of bony architecture. (**C**) Ventral view of caudal vertebrae; arrows indicate major vascular foramina. (**D**) Transverse section through one vascular foramen; arrow indicates site of entry of vascular tree.

cies and radiodensities makes an infectious process unlikely.

Mosasaurs are large (up to 13 m long) lizards that had a geologically short duration. The earliest known examples are early Late Cretaceous (Cenomanian) and the youngest Late Cretaceous (Maestrichtian), a time range from about 100 million to 64 million years ago. They are only known from sediments deposited under marine conditions and are all highly adapted for life in the sea.

Stomach contents are known from a few mosasaur specimens, although preserved contents are not common. It is clear that mosasaurs caught and ate fish as well as other vertebrates of suitable size. The occurrence of large ammonites with bite marks matching the teeth found on mosasaur jaws (*9*) indicates a preference for cephalopods—a preference shared with some of the living toothed whales. It is probable that the toothed whales, especially the early forms like zeuglodonts, are the animals with which mosasaurs can best be compared ecologically. We know that the modern sperm whale (*10*) has an affinity for giant squids, and similar but unrelated large squids are fairly common fossils in the same deposits that produce most of the mosasaur remains. It seems reasonable to suppose that these squids contributed to the diet of the contemporary mosasaurs, and in at least one case, this is verified by the stomach contents of a mosasaur.

Modern giant squids are thought to be predominantly inhabitants of deep water (*10*), and the sperm whales that feed on them are the deepest diving mammals. If we argue that Cretaceous squids also tended toward deeper water, then we might suppose that mosasaurs that feed on them might also be deep diving.

Mosasaurs generally are found in deposits of the epicontinental seas that covered much of the continents during the Cretaceous. Generally, these seas are thought to have been relatively shallow (100 m or less). However, depths of 1000 m or more may have developed in a few places. One of the most important of these epicontinental seas was the Kansas-Nebraska Sea that stretched from the Arctic Circle to what is presently the Gulf of Mexico and separated North America into east and west land masses. This ancient sea has produced the greatest number of fossil mosasaur remains known. Most are from the Niobrara Chalk in Kansas.

The Niobrara Chalk mosasaurs belong to three genera that show very different morphological adaptations and must have occupied somewhat different ecological regions. The tail is the main propulsive organ in mosasaurs. Although the tail may have been subjected to some compressional stress when the organism swam, its vertebrae were not load-bearing, as they are in the vertically upright human. The statistically significant difference in the prevalence of avascular necrosis between *Tylosaurus* and *Platecarpus* (Table 1) indicates either a difference in susceptibility, habitat, or behavior between the two genera. *Clidastes*, the smallest of the Niobrara Chalk genera, shows no incidence of avascular necrosis, whereas *Platecarpus*, the genus with the highest incidence, is intermediate between *Clidastes* and *Tylosaurus* in size. This indicates that a simple size factor is not involved. Vaughn and Dawson (*11*) argued for deep diving in *Platecarpus* on the basis of calcified tympanic membranes. It is possible that both the large *Tylosaurus* and the bulky *Platecarpus* more commonly visited deep water than did *Clidastes*.

The only pertinent causal factors of this pathology that can be evaluated in the fossil material relate to radiation, bismuth toxicity, and decompression sickness (*12*). Radiation toxicity, which requires substantial doses, may be the result of ingestion of radioactive material or exposure to a radioactive source. The former should result in some residual increase in the radioactivity of the bones. No systematic differences in radioactivity were noted between bones exhib-

Table 1. Prevalence of avascular necrosis in vertebrae of three genera of mosasaurs.

Genera	Individuals affected (%)	*n*	Involved vertebrae per specimen			
			Mean	SD	SEM	Range
Platecarpus	100	9	25.15	16.64	5.55	10–66
Tylosaurus	100	7	9.05	3.12	1.18	5–15
Clidastes	0	15				0

iting avascular necrosis and those of the *Clidastes* material that did not. Exposure to a radiation source is an interesting possibility because radiation bombardment is one suggested cause for Cretaceous extinctions (*13*). This probably would not be recognizable as an increase in bone radioactivity, but should have affected *Clidastes* also, and might be sought in other contemporary animals.

It is also known that bismuth poisoning can cause avascular necrosis (*14*); electron-probe analysis of some of the affected vertebrae failed to yield any significant concentrations. It is possible, however, that the diets of *Tylosaurus* and *Platecarpus* included organisms that concentrated some similarly toxic elements.

The most likely explanation for the high frequency of avascular necrosis in mosasaurs is caisson disease or the bends. Although whales apparently do not suffer bends, their anatomical modifications may not have been present in the mosasaurs. Young reported that whales store extra oxygen in the retea mirabile, an extensive blood vessel network (*15*). The high frequency of avascular necrosis in mosasaurs suggests that they lacked such an intravascular oxygen storage system. If such an oxygen-storage system was a later evolutionary event, the oxygen-storage system for mosasaurs may have been the air spaces of the lungs. This might have resulted in the equivalent of the scuba apparatus–associated phenomenon of avascular necrosis. The implications for mosasaurs transcend the bony phenomenon noted; the manifestations of avascular necrosis in man include symptomatology such as cerebrovascular accidents, which are detrimental to the organism's survival.

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Human Lymphocytes Making Rheumatoid Factor and Antibody to ssDNA Belong to Leu-1$^+$ B-Cell Subset

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B lymphocytes bearing the Leu-1 cell-surface antigen (Leu-1$^+$), the human equivalent of mouse Ly-1$^+$ B lymphocytes, have been detected in human peripheral blood, but there is little information on their frequency and properties. Analysis by fluorescence-activated cell sorter and double immunofluorescence showed that Leu-1$^+$ B cells are consistently present in the peripheral blood and spleens of healthy subjects and constitute 17.0 ± 5.0% (mean value ± standard deviation) and 17.3 ± 3.9%, respectively, of total B cells. When purified Leu-1$^+$ and Leu-1$^-$ B lymphocytes were transformed into immunoglobulin-secreting cells by infection with Epstein-Barr virus and the culture fluids were tested for reactivity with self-antigens, at least two important autoantibodies, antibody to the Fc fragment of human immunoglobulin G (rheumatoid factor) and antibody to single-stranded DNA, were found to be made exclusively by Leu-1$^+$ B cells. It is concluded that the Leu-1$^+$ lymphocytes represent a major subset of the normal human B cell repertoire and include the B cells capable of making autoantibodies similar to those found in systemic lupus erythematosus and rheumatoid arthritis.

THE LY-1 MARKER IS TYPICALLY EXpressed on the surface of all mouse T lymphocytes (Thy-1$^+$), including the helper and the suppressor/cytotoxic T cell subsets (*1*). The Ly-1 marker is also expressed on the surface of a minor subset of normal mouse B lymphocytes, albeit at a low density (*2–4*). In autoimmune NZB mice, this Ly-1$^+$ B cell subset is expanded and is responsible for the immunoglobulin M (IgM) "spontaneously" secreted in vitro by spleen cells (*3, 5*). These IgM include autoantibodies that react with single-stranded DNA (ssDNA) and thymocytes (*5*).

A fraction of human B lymphocytes from adult peripheral blood, lymph nodes, and tonsils were shown to express at low density the surface Leu-1 (CD5) molecule, the human equivalent of the mouse Ly-1 molecule (*6–10*). We have now used specific mouse monoclonal antibodies to Leu-1 and to human B lymphocytes in double-fluorescence flow cytometry to identify and quantitate Leu-1$^+$ B lymphocytes in peripheral blood and spleens from healthy adult subjects. Using in part a methodology we recently described (*11*), we separated Leu-1$^+$ B cells from their Leu-1$^-$ counterparts by cell sorting and infected the cells with Epstein-Barr virus (EBV), which transforms B lymphocytes into immunoglobulin (Ig)-secreting cells. Culture fluids were then investigated for Ig content and reactivity. The lymphocytes capable of producing autoantibodies similar to those found in at least two important human autoimmune diseases, systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), consistently segegated with the Leu-1$^+$ B cell subset.

The first set of experiments was designed to identify and quantitate Leu-1$^+$ B lymphocytes in healthy subjects. A mononuclear cell fraction enriched in B cells was prepared from human peripheral blood (*12*) and treated with phycoerythrin-conjugated mouse monoclonal antibody (PE-mAb, IgG2a) to B1 (CD20, a B cell marker) and biotin-labeled mAb (biot-mAb, IgG2a) to Leu-1. The cells were washed, incubated with fluorescein-conjugated avidin (FITC-avidin), washed again, and analyzed by fluorescence-activated cell sorter (FACS) (Fig. 1) for the presence of B lymphocytes bearing the Leu-1 marker. Figure 1D shows that approximately 14.0% of B1$^+$ cells (red fluorescence) also displayed the Leu-1 marker (green fluorescence). Leu-1 was expressed at low density on the surface of these B lymphocytes as indicated by their "dim" green fluorescence (cells within rectangle, upper right quadrant of Fig. 1D) as compared with the stronger fluorescence intensity of the residual T cells (Fig. 1D, lower right quadrant) also present in the material submitted for analysis. By this procedure, the percentage of Leu-1$^+$ B lymphocytes in the peripheral blood of 18 healthy subjects was measured. It was found that 9.0% to 26.6% (mean ± SD, 17.0 ± 5.0%) of B cells were Leu-1$^+$. Similarly, Leu-1$^+$ B cells represented 15.3% to 23.6% (17.3 ± 3.9%) of the B lymphocytes recovered from the spleen of six adult subjects. In other experiments, similar percentages of Leu-1$^+$ B lymphocytes were detected with different mAbs to

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