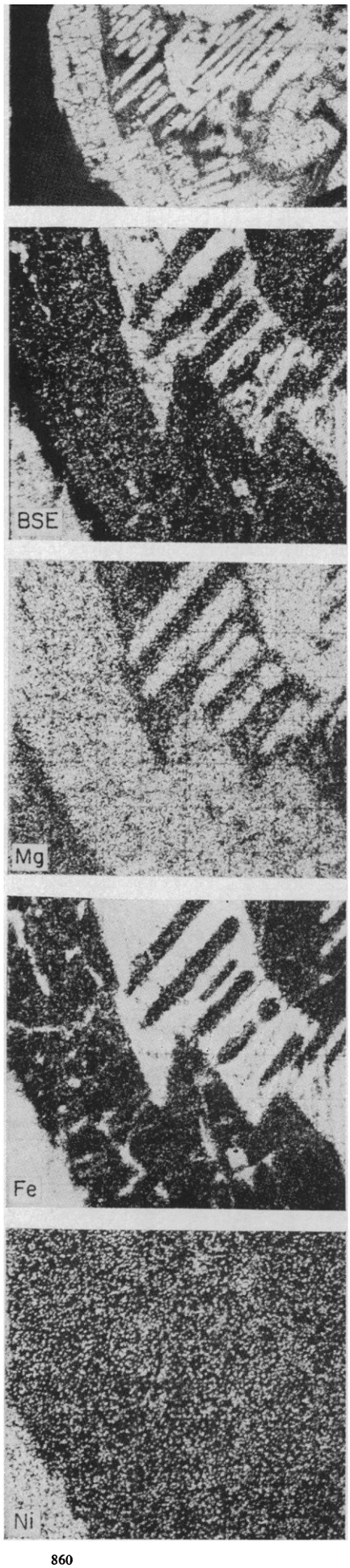

Fig. 6 (left). Photomicrograph and beam scanning pictures of part of a thin section of the Murray carbonaceous chondrite. BSE is a back-scattered electron image and Mg, Fe, and Ni show the distribution of these elements within the scanned area. The chondrule contains alternate lamellae of olivine and a darker, fine-grained, devitrified glass separated from the matrix by a rim of pyroxene. Olivine and pyroxene are both white in the Mg picture, while the devitrified glass with its relatively high iron content shows white in the BSE and Fe pictures. All the chondrule silicates contain much less nickel than the matrix. Scanned area is 250 by 250 μ.

ress, together with textural studies of chondrites, suggest that iron, nickel, and sulfur may be redistributed in a chondrite at temperatures well below the crystallization temperature of the silicates. The distribution of iron, nickel, and sulfur in chondrites may be controlled by both a high-temperature fractionation of contrasting phases and a low-temperature redistribution in the solid state.

The contrast in nickel content between the chondrule silicates and the matrix surrounding the chondrules is shown in Fig. 3. Figure 6 shows that a similar pattern exists in the carbonaceous chondrite Murray. The nickel distribution cannot be explained by an *in situ* transformation of either matrix into chondrules by solid-state recrystallization (*3*) or chondrules into matrix by weathering (*9*). The contrast in composition between matrix and chondrules in these meteorites implies that they are mechanical mixtures of materials formed under different conditions (*10*).

On the subject of meteoritic chondrules, Merrill (*11*) in 1929 wrote: "such interesting and peculiar forms are now known to be due to the cooling and partial crystallization of molten drops of stony matter; . . . their origin has been made the subject of much discussion and wordy warfare among students, but the matter need not be gone into further here." Concurrence with Merrill's conclusions and with the fact that iron was present when the chondrules solidified allows advance to the greater problem of the conditions under which these liquid droplets may form.

KURT FREDRIKSSON
Smithsonian Institution, Washington, D.C.

ARCH M. REID
Scripps Institution of Oceanography, La Jolla, California

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Radiocarbon Date from the Lake St. John Area, Quebec

Abstract. *A radiocarbon age of 8680 ± 140 years found for fossil marine shells in the Lake St. John area, Quebec, shows that marine submergence there apparently preceded the "Tyrrell Sea" in southeastern Hudson Bay, but followed the Champlain Sea episode in the St. Lawrence Lowlands.*

Fossil marine shells collected in the Lake St. John area of Quebec (48°31′N, 71°38′W) (*1*) (Fig. 1) have been dated at 8680 ± 140 years (*2*, *3*). The source of the shells is on the present 130-m contour above sea level (*4*); the bed, which is approximately 1 m thick, is overlain by 4 to 6 m of well-sorted sand which is locally cross-bedded. The uppermost part of the section appears to be windblown. *Hiatella arctica* accounted for about 80 percent of the fossil assemblage identified, the rest consisting of *Macoma balthica*. Because almost all the fossil shells had both valves together as in life, I assumed that they had not been transported far, if at all, before burial; the thickness of individual valves suggests that these mollusks had lived in an environment favorable as to salinity and temperature (*5*).

The shells are considered to be relatively shallow-water forms because of the sedimentary environment and because *M. balthica* is usually a shallow-water species.

In a search for further evidence of shallow-water environment, the line of direction of the long dimension of 100 shells of *H. arctica* was measured; no distinction was made between single valves and complete shells. The clear mode shown by the rose diagram (Fig. 1, inset) is here tentatively interpreted to indicate shallow-water environment; the long axes of the shells appear to be preferentially oriented perpendicular to a potential shore line. This would mean that, during the life of the mollusks, the water level at low tide was at or above the position of the present 130-m contour, depending on tidal fluctuations and the thickness of the layer of fresh water that presumably overlaid the salt water.

The date from this sample, GSC-313, is the first obtained from fossil shells in the Lake St. John area. However, radiocarbon dates obtained from comparable material in the main valley of the St. Lawrence indicate a maximum age of about 11,400 years (*6*). Elson and Karrow (*7*) have also traced the St. Narcisse end-moraine system as far east as the St. Anne River (Fig. 1).

On the basis of GSC-313, I suggest that the ice front extended across the Saguenay River valley or across both the Saguenay River and the Lake Kenogami valleys at the time of deposition of the St. Narcisse moraine, which is assumed to be in part contemporaneous with the Champlain Sea episode; thus, ice blocked marine waters from the Lake St. John basin.

It would follow that, when the St. Lawrence valley was already free of ice, the Lake St. John basin and adjacent areas to the south, including the Saguenay River valley, were still covered with ice; hence the brackish waters reached the Lake St. John basin later than the St. Lawrence valley. Furthermore, remnant blocks of ice or ice tongues may have persisted for some time in the Saguenay River valley and in the Lake Kenogami valley after the main ablation front retreated further to the north.

I have found, in the Lake St. John area, shells as high as 152 m above present sea level, but in quantities insufficient for dating; such shells might yield a greater age than that of GSC-313 and indicate the time of the maximum "marine submergence of the Lake St. John basin." However, if crustal warping amounts to 48 cm/km, as is common near the edge of the Canadian Shield, these shells may well be contemporaneous with the dated shells. Terasmae (*8*) has suggested that the marine episode in the main valley of the St. Lawrence was already terminated by 9000 years ago; however, late deglaciation, proximity of the Lake St. John area to the sea, and differential uplift may have caused the marine episode to persist later than in the St. Lawrence Lowlands.

Radiocarbon dates obtained by Lee *et al.* (*9*) in the James Bay Lowlands indicate that maximum submergence of the "Tyrrell Sea" occurred some 7000 to 8000 years ago. It would thus appear that the maximum extent of the marine invasion in the Lake St. John basin is older than the "Tyrrell Sea" maximum. It would then seem improbable that the Lake St. John basin was connected by a brackish waterway with the "Tyrrell Sea," as suggested by La Rocque (*10*), at least at the time of maximum submergence

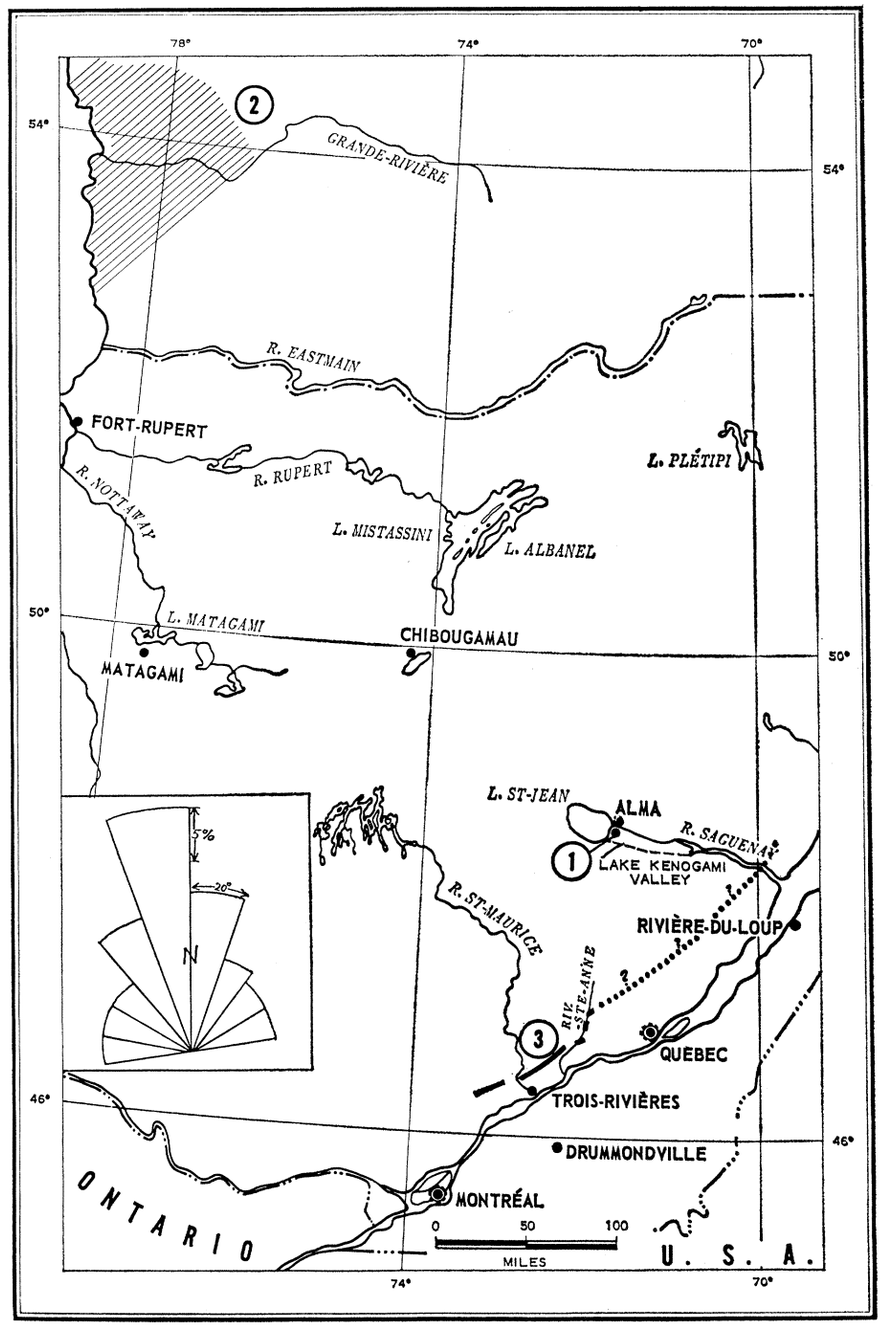

Fig. 1. Map of the general area. Sites: 1, GSC-313, shells; 2 (hatched), Lee's and other work mentioned in (*9*); 3, St. Narcisse end moraine, eastern part (*7*). Dotted line: extrapolated position of ice front at the time of deposition of the St. Narcisse moraine.

in both basins; moreover, meltwaters may have been too abundant to allow the brackish waters to even reach the northern part of the Lake St. John basin. However, GSC-313 does not invalidate La Rocque's idea.

PIERRE LASALLE
Quebec Department of Natural Resources, 1620 Boulevard de l'Entente, Quebec City, Canada

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12. Published by permission of the deputy minister, Quebec Department of Natural Resources.

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Cleft Palate Produced in Mice by Human-Equivalent Dosage with Triamcinolone

Abstract. *Triamcinolone produced cleft palates in mouse embryos at a dosage proportionate, by body weight, to common therapeutic dosage for humans. Thus, it showed much greater teratogenicity than other glucocorticoids tested on mice. Widely ranging doses of desoxycorticosterone did not produce cleft palates.*

Triamcinolone is used to treat diseases usually treated with glucocorticoids, especially dermatologic conditions. Hefley *et al.* (*1*) used triamcinolone for chronic allergic disorders such as asthma and chronic rhinitis in both male and female patients, 110 of whom were between the ages of 21 and 40. The effect of an intramuscular dose of 40 to 100 mg lasted for 40 days on average so that treatment of a mother before she knew she was pregnant could continue to exert an effect through the period of embryonic palate closure (33 days after the first missed menstrual period). The teratogenic effects of this drug should therefore be determined in relation to common human dosage. Fraser (*2*) reviewed the ratios of teratogenic dosage of various drugs, as applied to experimental animals, with therapeutic human dosage, on the basis of body weight; ratios ranged from 1 for tetracycline in rats to 400 for cortisone in mice. The figure of 400 may lead one to believe that there is a large margin of safety between teratogenic and therapeutic doses of glucocorticoids. This ratio is lower with some of the newer glucocorticoids, even allowing for their greater therapeutic effect per milligram in human beings (*3*, *4*). In this report we show that triamcinolone departs radically from the ratio of teratogenic to therapeutic dosage found with other corticosteroids.

Vaginal plugs were used as a criterion for timing pregnancies in 118 mice from matings within five inbred strains. From 11 to 14 days after conception, the pregnant mice were treated as follows: desoxycorticosterone acetate or desoxycorticosterone trimethylacetate was injected intramuscularly, triamcinolone diacetate was given by stomach tube, or triamcinolone acetonide was injected intramuscularly or subcutaneously. One or four daily injections were given at the times and dosages shown in Table 1. Uteri were removed at day 18 and fixed in Bouin's fluid. Fetuses were then removed and their palates were studied with a dissecting microscope after removal of the lower jaw. Average palate stage was calculated by assigning values of 0.25, 0.50, 0.75, and 1.00 to palate stages 1 (both shelves vertical), 3 (one shelf horizontal), 4 (both shelves horizontal), and 7 (normal palate), respectively (*5*).

Triamcinolone acetonide given intramuscularly to A/J strain pregnant mice on days 11 (11 days, 8 hours, assuming ovulation took place at 2 a.m.) to 14 caused excessive resorption in doses of 0.025 mg × 4 or higher (Table 1). Doses of 0.0125 to 0.001 mg/day caused cleft palates with frequencies ranging from 100 to 18 percent. The degree of inhibition of palatine shelf movement caused by triamcinolone over this dose range is reflected in the average palate stage (*5*), which increased from 0.55 to 0.96. Single doses of triamcinolone acetate also produced some clefts when injected on days 11, 12, and and 14.

The intramuscular, subcutaneous, and oral methods of administration were all effective, although triamcinolone diacetate given orally was less effective than triamcinolone acetonide given intramuscularly. Progression of the palatine shelves from a sagittal to a transverse plane was no greater with the subcutaneous than with the intramuscular method of administration, as shown by figures for average palate stage (Table 1). Cleft palate was induced by triamcinolone acetonide in strains C3H, C57BL, and DBA; strain 129/J was more resistant to the teratogenic effects of triamcinolone than strain A/J.

After administration of desoxycorticosterone, fetuses appeared normal in size and color. The three embryos with cleft lip–cleft palate do not constitute a frequency exceeding the expected spontaneous occurrence of 10 to 15 percent in the A/J strain.

Cortisone (*6*) and triamcinolone can best be compared for teratogenic potency at the highest dosage that causes cleft palates in 100 percent of offspring but does not cause a high frequency of resorption; this dosage would be 2.5 mg × 4 for cortisone (*6*) and 0.0125 mg × 4 for triamcinolone acetonide. The two teratogens produced almost identical average palate stages at such dosages (0.51 for cortisone and 0.55 for triamcinolone). Thus, 2.5 mg as opposed to 0.0125 mg represents a dosage difference of 200 times for teratogenic effect in mice, whereas these two glucocorticoids differ by a dosage factor of only about 6 times in therapeutic effect on man. Similarly, triamcinolone was 10 times more potent as a cleft-palate teratogen than dexamethasone, which was given in doses of 0.15 mg to produce cleft palate in 100 percent of the offspring of A/J strain mice (*4*). If we assume a weight difference of 2000 times between human beings and mice, the lowest dose of triamcinolone acetonide causing cleft palate in strain A/J mice, 0.001 mg × 4, would be equivalent to a dose of 2 mg/day for 4 days in human beings; this dosage is well within the recommended therapeutic range.

The relative roles of anti-inflammatory and salt-retention effects of glucocorticoids should also be investigated. There are reasons for implicating the latter effect in the report of changes in amount of amniotic fluid associated with treatment by cortisone and certain other teratogens that produce cleft palate (*7*);