The occurrence of hematopoietic bone marrow within the axial skeleton and metaphyseal regions of long bones is well known. However, it has been generally accepted that hematopoietic marrow is not present within the epiphysis of long bones in normal adults. This study involved evaluation of marrow patterns in 96 patients presenting for shoulder magnetic resonance (MR) imaging examinations. Residual hematopoietic marrow was present within the proximal humeral metaphysis in 99% of patients and extended into the epiphysis in 62%. Epiphysial hematopoietic marrow was more prominent in female subjects (P = .015) and showed correlation with prominence of hematopoietic marrow within the proximal humeral metaphysis (P = .01). The most characteristic pattern was a curvilinear distribution of hematopoietic marrow involving the subcortical region of the medial humeral head, though in some patients more centrally located patchy or globular regions of hematopoietic marrow were observed. These findings indicate that when signal intensity variations are observed within the epiphysis on MR images, the possibility of residual or reconverted hematopoietic marrow should be considered.

**Magnetic Resonance Imaging** (MR imaging is highly sensitive for depiction of bone marrow lesions. This is due to the inherent ability of MR to demonstrate signal intensity alterations of lesions as distinct from those of surrounding normal marrow fat. Variations in marrow signal intensity on MR images may also reflect the regional distribution of normal hematopoietic and fatty marrow populations (1). The distribution of hematopoietic and fatty bone marrow varies according to skeletal site, patient age and sex, and pathologic condition. Awareness of the patterns of hematopoietic marrow distribution is important so that physiologic hematopoietic marrow is not mistaken for marrow disease (2).

In the adult, it is widely recognized that residual hematopoietic marrow is present throughout the axial skeleton. In addition, hematopoietic marrow is usually present within the proximal metaphyses of the femur and humerus (3–5). However, there have been conflicting statements regarding the presence of hematopoietic marrow within the epiphysis of normal adults. The objective of this study was to address the issue of whether residual hematopoietic marrow is observed within the epiphysis on MR images.

**MATERIALS AND METHODS**

Retrospective review of 100 consecutive patients presenting for shoulder MR examinations was performed. There were 64 male and 36 female subjects, with a mean age of 41 years (range, 13–83 years). When patients were categorized according to age, there were 13 patients younger than 20 years, 14 patients between 21 and 30 years, 22 patients between 31 and 40 years, 21 patients between 41 and 50 years, 20 patients between 51 and 60 years, and 10 patients greater than 61 years of age. All patients presented for evaluation of possible tears involving the rotator cuff and/or glenoid labrum. There was no known history of primary or metastatic bone malignancy in any of these patients, nor was there clinical, radiographic, or laboratory evidence to suggest the presence of fracture, osteomyelitis, ischemic necrosis, or other forms of marrow disease involving the shoulder.

Examinations were performed with a 1.5-T superconducting system (GE Medical Systems, Milwaukee, Wis). A local coil (Medical Advances, Milwaukee, Wis) was placed over the shoulder to improve signal-to-noise ratio. Coronal oblique images were acquired with use of T1-weighted (repetition time msec/echo time msec = 650/18, two excitations) and spin density/T2-weighted (2,200/20,70; one excitation) parameters. The latter sequence was also repeated with use of fat saturation, with all other parameters held constant. A section thickness of 4 mm was used, with a 0.5-mm intersection gap, 192 x 256 matrix, and 16-cm field of view. Artifact control methods included spatial presaturation and respiratory-ordered phase encoding.

These images were used to analyze the marrow signal intensity patterns within the proximal humerus. The presence of fatty marrow was determined when the marrow space demonstrated increased signal intensity on T1-weighted images and moderate signal intensity on T2-weighted images. Correlation of marrow signal intensity with the signal intensity of subcutaneous fat and suppression of signal intensity on fat-suppressed images allowed confirmation of fatty marrow. The presence of hematopoietic marrow was determined when areas that were hypointense relative to fat on T1-weighted as well as T2-weighted images and that were approximately isointense with skeletal muscle were seen with all pulse sequences (6–8).

In three patients, areas of marked hyperintensity on T2-weighted images were observed that appeared to represent posttraumatic marrow edema. These patients were excluded from the study. One additional patient was excluded due to severe motion artifacts that obscured adequate visualization of marrow signal intensity patterns. The observation of small discrete subchondral cysts along the posterosuperior humeral head was not used as an exclusionary criterion.

The marrow distribution patterns within the proximal humeral metaphysis...
and epiphysis were separately analyzed for the remaining 96 patients. For each region, the location and pattern of hematopoietic marrow were recorded descriptively and with use of a schematic diagram. In addition, the diameter of the epiphysis and/or metaphysis that was occupied by hematopoietic marrow was measured with calipers, as was the diameter of the humerus at that corresponding location. These measurements were used to calculate a percentage of hematopoietic marrow involvement for both the humeral epiphysis and metaphysis. The presence of MR findings indicating partial- or full-thickness tears of the rotator cuff were noted, with standard diagnostic criteria used.

The prominence of epiphyseal and metaphyseal hematopoietic marrow was analyzed for possible correlation with patient age, sex, and presence of rotator cuff tear. In addition, the prominence of hematopoietic marrow within the metaphysis and epiphysis was evaluated for possible correlation. Statistical analysis involved calculation of the Pearson correlation coefficient \( r \), as well as calculation of \( P \) values with use of a \( t \) test. \( P \) values less than or equal to .05 were considered statistically significant.

RESULTS

Hematopoietic marrow was present within the proximal humeral metaphysis in 95 of 96 patients (99%). The single patient without evidence of metaphyseal hematopoietic marrow was a 76-year-old man. The mean percentage diameter of the metaphysis that contained hematopoietic marrow was 82.8%, with a standard deviation of 28.2%. There was a significant inverse correlation between prominence of metaphyseal hematopoietic marrow and patient age \( (r = - .38, P = .0001) \). There was no significant correlation between prominence of metaphyseal hematopoietic marrow and patient gender \( (r = .19, P = .061) \). Similarly, no significant relationship between prominence of metaphyseal hematopoietic marrow and the presence of a partial- or full-thickness rotator cuff tear was found \( (r = -.06, P = .56) \).

The location of hematopoietic marrow within the metaphysis was most frequently diffuse (66 of 96 patients, 69%) (Figs 1-3). There was a predominance of hematopoietic marrow along the medial aspect of the metaphysis in 22 patients (23%). Hematopoietic marrow was concentrated within the center of the metaphysis in three patients (3%). Prominent foci of hematopoietic marrow were present separately within both the medial and lateral aspects of the metaphysis in three patients (3%) and within the central and lateral metaphysis in one patient (1%).

The predominant morphologic pattern of hematopoietic marrow involvement within the metaphysis was confluent in 44 of 96 patients (46%). In 39 of 96 patients (41%), there was a patchy distribution of hematopoietic marrow within the involved portion of the metaphysis. Linear orientation of metaphyseal hematopoietic marrow was observed in 12 of 96 patients (12%).

Epiphyseal hematopoietic marrow was visualized in 60 of 96 patients.
(62%). In patients with evidence of epiphyseal hematopoietic marrow, the percentage of the epiphyseal diameter in which hematopoietic marrow was present ranged from 4% to 100%, with a mean of 20%. The overall mean percentage involvement regarding epiphyseal hematopoietic marrow for the entire population of 96 patients was 12.5%, with a standard deviation of 16.4%. There was no significant correlation between prominence of epiphyseal hematopoietic marrow and patient age ($r = -0.04, P = .70$). However, epiphyseal hematopoietic marrow was significantly more prominent in female than male subjects ($r = .25, P = .015$).

Epiphyseal hematopoietic marrow was not significantly correlated with the presence of rotator cuff tear ($r = .12, P = .24$). There was a significant correlation between prominence of hematopoietic marrow within the metaphysis and within the epiphysis ($r = .26, P = .01$).

The location of epiphyseal hematopoietic marrow was confined to the immediate subcortical region of the medial humeral head in 38 of 96 patients (40%) (Fig 1). In two of 96 patients (2%), the presence of hematopoietic marrow continued to be evident along the subcortical region of the apical portion of the humeral head. In two additional patients (2%), hematopoietic marrow was observed along the entire subcortical extent of the humeral head. Concurrent involvement of the subcortical medial epiphysis in conjunction with involvement of the more central medullary region of the medial, lateral, or apical portions of the humeral epiphysis was observed in two patients (2%), one patient (1%), and two patients (2%), respectively. Hematopoietic marrow was confined to the medial, lateral, or apical portions of the central humeral epiphysis (excluding the subcortical region) in seven patients (7%), one patient (1%), and two patients (2%), respectively (Fig 2). In two patients (2%), there was concurrent involvement of the medial and lateral aspects of the humeral head, and in one patient (1%) scattered foci of hematopoietic marrow were present diffusely throughout the humeral epiphysis.

The morphologic pattern of hematopoietic marrow involvement of the humeral epiphysis was curvilinear in 30 patients (31%) (Fig 1). This pattern was observed in patients who demonstrated hematopoietic marrow within the subcortical region of the epiphysis. In nine additional patients (9%) with a curvilinear pattern, there were also linear foci of hematopoietic marrow that were oriented perpendicular to the medial curvature of the humeral head, which extended centrally. A curvilinear pattern was combined with additional foci of patchy or confluent hematopoietic marrow involvement in four patients (4%) and two patients (2%), respectively. An isolated pattern of patchy, confluent, linear, or globular hematopoietic marrow involvement was observed in 11 patients (11%), two patients (2%), one patient (1%), and one patient (1%), respectively.

The rotator cuff was of normal appearance in 43 patients. There was evidence of a partial- or full-thickness tear of the cuff in 19 and 18 patients, respectively. Plain radiographs of the shoulder were available for review in 20 patients and in all cases demonstrated no abnormalities that corresponded to the regions of apparent hematopoietic marrow on MR images.

**DISCUSSION**

The entire marrow space is composed of hematopoietic (ie, red, cellular, or active) marrow throughout most of fetal life. The process of conversion from hematopoietic to fatty (yellow or inactive) marrow begins within the terminal phalanges shortly before birth (3,9). Marrow conversion continues to proceed throughout childhood and adolescence, initially involving distal bones and subsequently progressing to more proximal portions of the appendicular skeleton (3). The stimulus for marrow conversion is not completely understood; this process appears to be mediated by alterations in body temperature, the vasculature, oxygen tension, aging, and possibly other factors (3,4, 7,10).

An adult marrow pattern is reached by 18–25 years of age (3,10,11). In adults, residual hematopoietic marrow is present throughout the axial skeleton, including the skull, facial bones, spine, sternum, and pelvis (3,9,10,12). The appendicular skeleton is occupied primarily by fatty marrow, except for rests of hematopoietic marrow within the proximal humeral and femoral metaphyses (12). Reconversion of fatty to hematopoietic marrow may occur throughout the axial as well as appendicular skeleton in response to anemia or marrow replacement. Marrow reconversion usually progresses in a proximal to distal direction.

MR is inherently sensitive in depiction of normal bone marrow distribution patterns (4). Superb differentiation between hematopoietic and fatty bone marrow is provided on T1-weighted spin-echo images (7,13,14). T1-weighted images depict fatty marrow as significantly hyperintense, as contrasted with the relative decreased signal intensity of hematopoietic marrow components. These differences in signal intensity are a direct reflection of the differences in composition of hematopoietic and fatty marrow. Hematopoietic marrow consists of approximately 40% water, 40% fat, and 20% protein, whereas fatty marrow contains 80% fat, 15% water, and 5% protein (9). The greatly increased fat content of fatty marrow contributes to shortening of T1 relaxation and is responsible for its relative hyperintensity on T1-weighted images (4).

Knowledge of hematopoietic and fatty bone marrow distribution patterns is important for accurate interpretation of MR images. This is because the appearance of hematopoietic marrow may overlap that which is demonstrated by various types of marrow lesions (2,15–17). Specific types of marrow lesions are also known to preferentially involve
sites populated by either fatty or hematopoietic marrow (3,6,18). Because of this, knowledge of marrow distribution patterns is of even further value for differential diagnosis of abnormalities detected on MR images (14). Recognition of abnormal marrow reconversion also relies on familiarity with normal patterns of hematopoietic marrow distribution (16).

The objective of this study was to determine if residual hematopoietic marrow is present within the epiphysis of normal adult subjects. The prevailing view is that the adult epiphyses contain exclusively fatty marrow and are essentially devoid of hematopoietic marrow (1,4,5,6,13,14,16,18,19). Consequently, it has been stated that the normal appearance of the epiphyses on T1-weighted MR images is that of uniform hyperintensity. Any focus of relative hypointensity within the epiphysis of adults has been regarded as evidence of disease (17). Lesions that may involve the epiphyses include avascular necrosis, fracture, primary bone tumor (20), metastatic tumor (19), osteomyelitis, and benign or malignant infiltrative marrow disorders. The presence of fat signal intensity throughout the epiphyses has also been used as a criterion with which to distinguish hyperplastic hematopoietic marrow from diffuse neoplastic marrow involvement. This is based on the premise that the epiphyses lack hematopoietic potential and thus do not usually participate in the process of marrow reconversion.

The results of this study indicate that residual hematopoietic marrow is frequently present within the proximal humeral epiphysis of normal adults. These findings are in agreement with those of Custer, who stated that hematopoietic marrow persists to some extent in the proximal epiphyses of the femur and humerus throughout life (10). In addition, Pinney observed histologically that a few small patches of hematopoietic marrow may be visible within the epiphyses throughout life (11).

Hematopoietic marrow was usually observed in a curvilinear distribution along the subcortical aspect of the medial humeral head. This correlates directly with the pattern of hematopoietic marrow distribution that has been displayed in cadaver sections in several anatomic atlases (21,22) (Fig 3). Predominance of residual hematopoietic marrow near the subcortical region of the medullary cavity has been previously noted (11). The marrow space is conceived of as being divided into wedge-shaped functional units. Hematopoietic marrow usually occupies the periphery of these units, with fatty marrow located more centrally (23). The presence of trabecular bone and signal intensity variations related to distance from a surface coil or uneven fat suppression may also result in altered marrow signal intensity. However, these entities did not appear to contribute to the findings that I observed.

A recent report by Jaramillo et al described the frequent observation of hematopoietic marrow within the epiphyses of infants on MR images (17). This appearance was observed when the estimated age of the epiphyseal ossification center was 8 months or less. The presence of epiphyseal hematopoietic marrow was confirmed histologically in infant animals in this same report. Moore and Dawson (16) observed foci of intermediate signal intensity on T1-weighted images within the femoral capital epiphysis in several subjects. They attributed these findings to partial volume averaging of marrow fat with adjacent bone cortex in most subjects, although in two subjects this did not appear to be an adequate explanation. They speculated that reinforcement of bone trabeculae along the weight-bearing axis of the femur might contribute to these signal intensity variations.

In an earlier article (24), I made a preliminary observation of hematopoietic marrow within the epiphysis of normal adults on MR images. Previous investigations of hematopoietic marrow patterns within the appendicular skeleton have focused almost exclusively on the proximal femur. It is known that the adult humerus contains a larger quantity of hematopoietic marrow than the femur (11). Furthermore, most previous studies that evaluated marrow distribution patterns used images acquired with a body coil and relatively large fields of view. In the current investigation, a surface coil was used to achieve high signal-to-noise ratio, and relatively small voxel sizes were obtained. The explanation for the lack of observation of epiphyseal hematopoietic marrow in previous studies may be related to these two considerations.

Familiarity with established patterns of hematopoietic marrow distribution is of critical importance in distinguishing between hematopoietic marrow and marrow lesions on MR images. There are several additional observations that may also be useful in this regard. Hematopoietic marrow does not result in significant hyperintensity on images acquired with T2-weighted, fat-suppressed T2-weighted, or short tau inversion re-

Figure 4. T1-weighted MR images of the shoulders in two separate patients with severe anemia. There is confluent reduced signal intensity due to reconversion of fatty to hematopoietic marrow throughout the humeral epiphyses bilaterally in both patients.
Reconversion of fatty to hematopoietic marrow may occur within the epiphysis, although this event appears to occur only in the presence of relatively severe anemia and/or marrow replacement (5,6,25) (Fig 4). In an analysis of femoral marrow patterns in 14 patients with polycythemia vera and myelofibrosis, Kaplan et al observed hematopoietic marrow within the femoral capital epiphysis in 10 patients (13). In two patients in their series, epiphyseal/apophyseal marrow appeared more cellular (ie, less intense on T1-weighted images) than marrow within the proximal metaphysis.

This study involved analysis of a quasi-normal population, as patients presented with shoulder pain. However, there were no known predisposing factors that would result in marrow disease in these patients. It is highly unlikely that the underlying reason(s) for shoulder pain in these patients would influence marrow patterns in the shoulder. This was validated by the lack of correlation between hematopoietic marrow prominence and rotator cuff disease.

In conclusion, residual hematopoietic marrow may be observed within the proximal humeral epiphysis in normal adults, and the epiphyses may participate in the process of marrow reconversion due to anemia or marrow replacement disorders. Epiphyseal signal intensity variations on MR images may reflect the presence of hematopoietic marrow and do not necessarily indicate disease.

References