CHANGES IN MUSCULOSKELETAL SYSTEM AFTER IMMOBILIZATION

Abstract

With this review our team would like to draw the attention to some of the most common changes which take place in musculoskeletal system after immobilization and bedrest (IB). IB are frequent and inseparable part of the treatment process following a variety of medical conditions. Even considered imperative to protect and/or to support the injured part of the body, in certain situations, IB can cause many physiological and clinical deleterious effects. Not only the contractile tissues are affected negatively by IB - the same applies for the noncontractile as well – namely the bones, ligaments, synovium and cartilage. Although the changes in deep located tissues are not so easily noticeable at first sight (compared with the loss of muscle mass for instance), they do exist and lead to more or less serious limitations and delays during the treatment process.

Keywords: bones, cartilage, contracture, ligament, muscles

Introduction

Synovium

Synovial fluid lubricates the ligamentous structures of the joint and provides nourishment to the cartilage, menisci, and ligaments and motion enhances the trans-synovial nutrient flow. Some of the most prominent changes after IB can be summarized as follows - proliferation of fibrofatty connective tissue within the joint space, adhesions between synovial folds, and adherence of fibro-fatty connective tissue to cartilage surfaces and tearing of the latter when forced manipulation is applied. The proliferative fibrofatty connective tissue covers intraarticular soft tissue and it also blankets the non-articulating cartilage surfaces. With time, adhesions develop between the exposed tissue surfaces as the fibrofatty connective tissue is transformed into more mature scar. Last but not least, the range of motion (ROM) on an arthrography indicates that the force required for the first extension-flexion cycle, is increased more than 12 fold.[1]

Ligament and ligament insertion side

By dry mass, ligaments are 70% to 80% collagen. Collagen is arranged within the ligaments in parallel bundles (fascicles), oriented along the axis of the limb. Unlike tendons, ligament structures contain elastin (3% - 5%), seemingly to compensate for their rigid proximal and distal attachments.[1] During IB, evident are the disorganization of the parallel arrays of fibrils and cells and destruction of the ligament fibers attached to the bone as a result of the osteoclastic activity. Stress-strain diagrams of collateral ligaments show increased deformation with a standard load, i.e., greater compliance.[1]

The extent and severity of the alterations in ligaments depend to certain extent on the type of insertion. In generally we can divide the insertions into two types – direct/bony and indirect/periosteal. As an example, for the first type are the ACL's tibial and femoral attachments - most of the collagen fibrils pass directly into the bone matrix. As for the second type of insertions, many of the collagen fibrils join the periosteum and relatively few fibrils pass obliquely into the bone matrix, e.g. the medial collateral ligament of the knee.[2, 1]

Decreased ligament loading due to immobilization usually produces more extensive changes in the indirect/periosteal insertions – subperiosteal osteoclasts resorb much of the bony insertion of ligaments subjected to prolonged immobilization. In the direct/bony insertions, the resorption occurs around it, but relatively small resorptive activity occurs within the insertion.[2]

Prolonged immobilization causes bone resorption around the periphery of the cruciate ligament insertions, but only limited resorptive activity beneath the insertion site and in the zone of mineralized fibrocartilage. In contrast,

prolonged immobilization causes significant diffuse resorption of the bony part of tibial insertion of the medial collateral ligament. These changes, particularly those in the indirect/periosteal insertions, weaken the bone-ligament junction significantly within 6 to 8 weeks.[2]
A recent study by Matsuzaki et al.[3] supports these statements adding the conclusion that the duration of immobilization should be limited to less than one month to minimize degeneration of the ACL insertion and the articular cartilage. The authors discovered that knee immobilization significantly increased chondrocyte apoptosis in the ACL insertion at 2 and 8 weeks after surgery and in the tibial articular cartilage at 4 and 8 weeks after surgery respectively.
In Videman's[4] study has been proposed a hypothesis for the role of periarticular soft tissues in joint degeneration which addresses one possible mechanism for the development of osteoarthritis (Fig. 1). The authors pointed out the increased fibrosis of periarticular tissues, cartilage proliferation at joint edges, atrophy at weight-bearing areas, and regional bony eburnation, sclerosis and resorption that can be found after two weeks of immobilization.

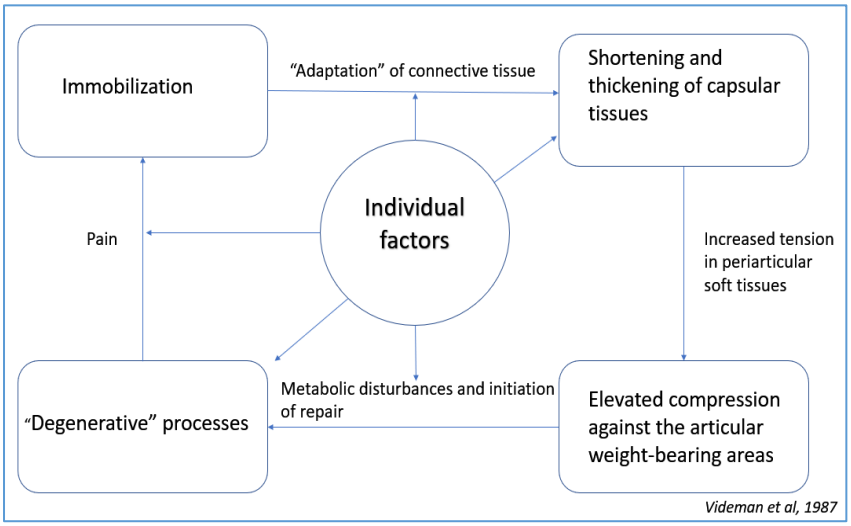

Fig. 1 Hypothesis for role of periarticular soft tissues in joint degeneration[4]

Bones

Bone is a dynamic tissue that undergoes continuous remodeling, in response to the dual stimuli of weightbearing and muscle pull. During and after IB, calcium loss from bone begins immediately and increased urinary clearance of calcium is detectable within a few days. More gradual calcium loss accompanies the declining activity of age or chronic-illness and accounts for the frequency of hip and vertebral fractures in the elderly.[5]
Bone is generally classified into two types: cortical bone, also known as compact bone; and trabecular (cancellous) bone, also known as spongy bone. Cortical bone is dense and is found in the shaft of long bones and trabecular one is much more porous and is found in the end of long bones, in vertebrae and in flat bones such as the pelvis.
During immobility, both cortical and trabecular bones are lost. Since the loss is predominantly of trabecular bone, it occurs mainly in weight-bearing bones - the vertebrae, the long bones of the legs, the heels and wrists. Bone mineral density of the vertebral column decreases by about 1% per week of bedrest, nearly 50 times that of normal age-related bone loss.[6]
A study by Rittweger et al.[7] concluded that the losses in BMC (bone mineral content) continues after the end of the bed rest and it is not clear how long this loss would continue and when the actual peak occurs.
Reduced activity may not produce readily detectable changes in bone volume, shape and strength, but prolonged immobilization of a limb will cause radiographic changes including decreased density of cancellous bone, loss of trabeculae, thinning and increased porosity of cortical bone and drastic reduction in the mineral content. These alterations diminish bone strength and rise the probability of a fracture causing disuse osteoporosis[6, 1]. Regaining bone density after prolonged IB, even with vigorous activity, requires many months, even in children. In some individuals, especially elderly, bone density may never return to its previous level[2] A recent rat study by Lin et al.[8] reveals in details the changes in skeletal tissues after SCI (spinal cord injury) and the subsequent deprivation

of mechanical stimuli. The bone loss following SCI, far exceeds that induced by other insults, such as estrogen deficiency, neurological deficit and mechanical unloading. The local factors (immobilization and bone denervation) affect more the trabecular bone and the systemic factors (hormonal and metabolic changes) affect primarily the cortical bones.
Some images from that study perfectly illustrate the control and SCI group's changes in femur, humerus and vertebral body of L4 respectively (Fig.2-4).

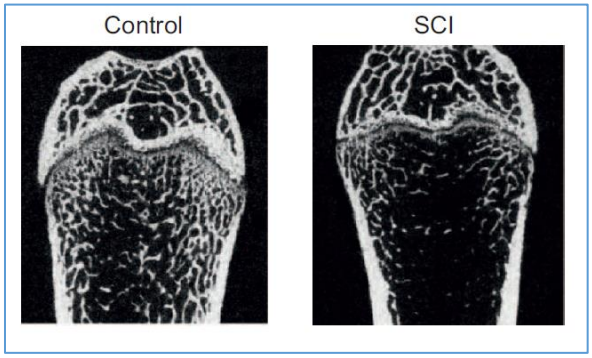

Fig.2 - Femur

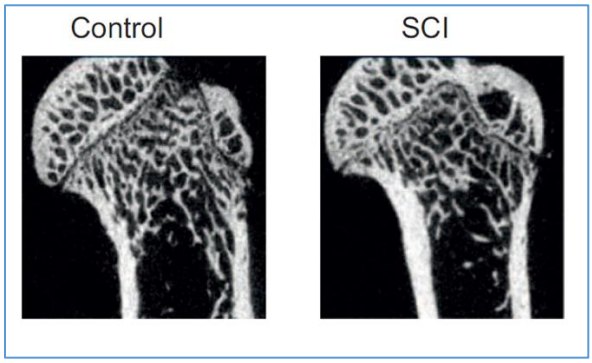

Fig. 3 – Humerus

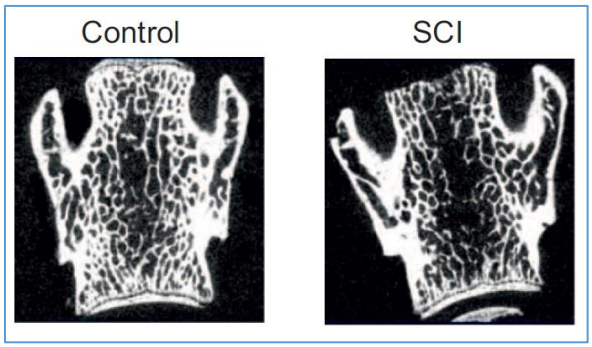

Fig.4 – Vertebral body L4

Cartilage

The changes affecting articular cartilage can be divided into 2 groups - those in non-contact areas, and those in contact areas. The changes in the non-contact areas are thought to be secondary to the fibrofatty connective tissue proliferation described above. The ingrowth of connective tissue which fills the joint space soon covers the joint surfaces. In the contact areas, mild to severe changes of articular cartilage are observed depending on the rigidity of immobilization, the position of immobilization, and most important - the degree of compression. In areas with greater compressive forces there are varying degrees of destruction including full thickness ulceration of cartilage

with cellular distortion and necrosis, fibrillation of matrix, and erosion of matrix down to subchondral bone. Hyperemia in the subadjacent marrow spaces is noted with proliferation of vascular connective tissue. In some areas this tissue penetrates the subchondral plate and hinders the calcified layer of articular cartilage. Trabecular atrophy and resorption in the areas subadjacent to cartilage lesions are also seen. Subchondral cysts sometimes develop in this location in animals followed for longer periods.[9, 1]

Recent animal study pointed out important clinical findings namely that osteoarthritis (OA) also developed in the contralateral non-immobilized limb. The roughness of articular cartilage was observed visually in the immobilized knee (experimental knee) after 2 weeks of immobilization, and cartilage degeneration developed following immobilization. In the contralateral knee, cartilage surfaces demonstrated degenerative changes after 4 weeks, suggesting that immobilization caused joint surface degeneration in both immobilized and contralateral knees. (Fig. 5)

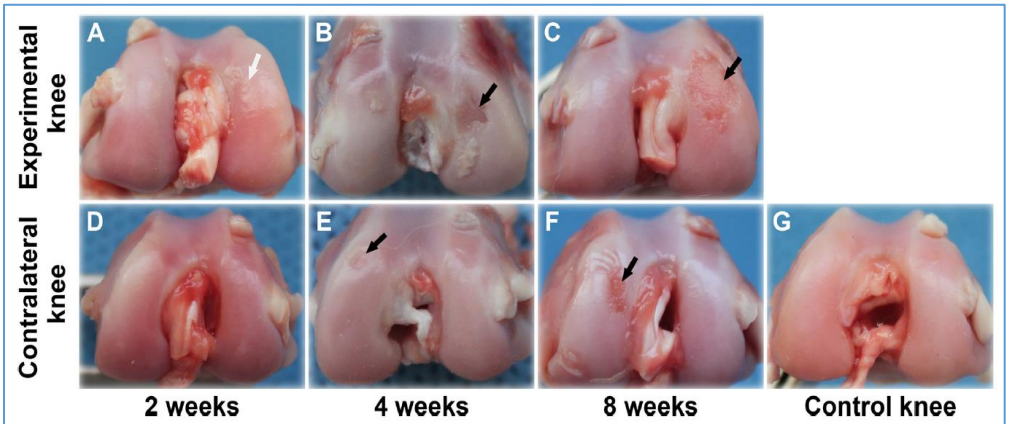

Fig. 1 Macroscopic observation of cartilage specimens after immobilization. **a-c** Experimental knees; **d-f** Contralateral knees; **g** Control knee. White arrows: roughness of the cartilage surface. Black arrows: cartilage defect

Fig.5. Zhou et al. [10]

Contracture

The joint contracture is the most frequent complication after IB, and a result of shortening both connective tissue and muscles.[11]

Contractures may be anticipated side effects of a necessary treatment and some contractures are produced unwittingly and unnecessarily - for example the frozen shoulder caused by the use of a sling to treat a Colles' fracture of the wrist. Contractures probably begin forming within 8 hours, as illustrated by the morning stiffness after a night's sleep, but this can be reversed by a single range of motion exercise.[5] However, 2 to 3 weeks of immobilization will produce a much firmer contracture, and this is a frequent complication of bedrest.[6]

The rate of contracture formation is accelerated by several factors that often may coexist in the immobilized parts: oedema, bleeding, infection, burns, or the healing of traumatic or surgical wounds.[5]

There are additional contributing factors such as:

- Improper bed - resulting in deformities, particularly in joints of the lower extremities.
- Adaptive shortening of soft tissues when the limb is held in a shortened position (e.g., in a cast) might occur.

Contractures are most commonly seen in individuals with joint diseases or paralysis of a muscle group or in elderly individuals who are frail, cognitively impaired, or very passive.[12]

Contractures may be prevented through proper positioning and the use of straps and supports. Carrying each joint through its full range of motion at least once every eight hours is the key to prevention of contractures.[5]

This was proposed in animal study by Jarvinen et.al.[13] where the team suggest that immobilizing the gastrocnemius muscle-tendon unit in a lengthened position causes less muscle atrophy and less decrease in tensile properties than immobilizing in a shortened position.

Muscles

Changes in the muscle tissue have been demonstrated to exist as early as 2 days post-immobilization.[14] The earliest change that includes swelling of the sarcoplasmic reticulum 5 days post-immobilization, shows that

sarcomeres are extremely distorted. In some cases, fibers near the proximal and distal end regions of the muscle, show greater changes than those seen in the mid-belly region. Four weeks after immobilization there is an irregularity and considerable distance between contractile elements and fibers, as well as changes in fiber size, shape and loss of muscle mass. Z-discs within the muscle are distorted and located obliquely or longitudinally. After 8 weeks of immobilization Z-discs appear to be randomly oriented. At the end of 14 weeks, the muscle is significantly altered in comparison with normal.[15] The muscle become extremely disorganized with significant loss of fiber mass and a decrease of dry weight. There is a loss in tension generating capabilities. Immobilisation in a shortened position was associated with a significantly greater decrease in length and weight than was immobilisation in a lengthened position.[16]

–Another evidence is that the number of sarcomeres significantly decreases in young individuals with developing muscles which are immobilized also in shortened position. Changes in muscle are apparent histologically and manifested functionally. Loss of muscle mass and the change in number of sarcomeres significantly decreases a muscle's function ability in terms of generation of tension.[17]

A muscle is only as strong as it needs to be for the tasks it regularly does. Disuse atrophy leads to the loss of about an 1/8 of muscle's strength per week of total inactivity. A partially used muscle exerting less than 20% of its maximum force will begin to atrophy, whereas regular exertion at 20% to 30% of maximum force will preserve a muscle's strength. [5] Anti-gravity muscles such as leg extensors and trunk musculature are preferentially affected by the loss of mechanical loading compared to hand and upper limb musculature.[18, 19] De Boer et. al.[20] notes that in a 23 days program a limb suspension model, muscle mass was seen to reduce by 5,2% within the first 2 weeks and subjects lost in total 10% of quadriceps muscle mass by 23rd day. In several studies, a period between 10 and 14 days have been enough to observe relatively small decreases in muscle mass. [21, 22] Decreased muscle protein synthesis (MPS) was demonstrated by Gibson using a limb casting method, over a period longer than 6 weeks.[23,24] Fernando et al.[25] demonstrated loss of muscle mass within 7 days. Additionally to an overall reduction in muscle mass, there is a reduction in muscle fiber size[18, 19] with accelerated reduction in the strength of fast-twitch (Type II) fiber compared to slow-twitch (Type I) fibers which rely on oxidative metabolic process, resulting in lower fatigue resistance capacity. [18, 26] They found that there is not only a loss of muscle force generation capacity due to a reduction in muscle mass and contractile proteins, but also alterations in muscle electromyographic activity. This highlighted changes occur in terms of the neural or muscle membrane excitability to enable potentiation of a muscle contraction.[27, 28] Immobility also increases the production of pro-inflammatory cytokines and reactive oxygen species with subsequent muscle proteolysis promoting overall muscle loss.[11, 29] As a result of loss of muscle mass, up to 40% of muscle strength can be lost within the first two weeks of immobilization.[18] Another study shows a preferential atrophy of the anti-gravity muscle groups such a soleus, back extensors and quadriceps musculature. Fiber atrophy may relate to the initial fiber size, which may explain partly why anti-gravity musculature which consist primarily of Type I fibers preferentially atrophies. Loss of muscle contractile protein and fiber size is only one component to the loss of force generation capability. Other factors which interplay include neural, hormonal and cellular signaling processes.

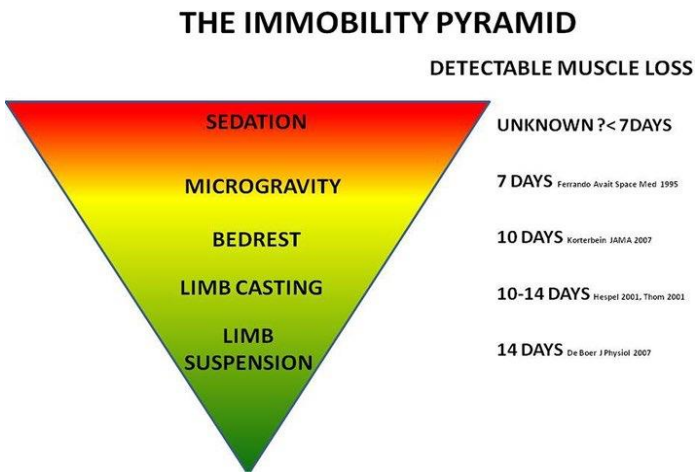

Fig. 6 The immobility period. Providing conceptualization of the rate of muscle wasting in different states of immobilization based on the research literature. [30]

The loss of sarcomeres and reduction in muscle length, according to Williams and Goldspink[17], which occurs when muscles are working at a shortened length, is associated with an increased resistance to passive stretch. The amount and arrangement of connective tissue in the perimysium and endomysium is expected to affect muscle elasticity. Increased stiffness of immobilized muscle could be accounted for by an increased collagen content and determine whether any increase is mainly in the endomysium or in the perimysium (Fig.7).

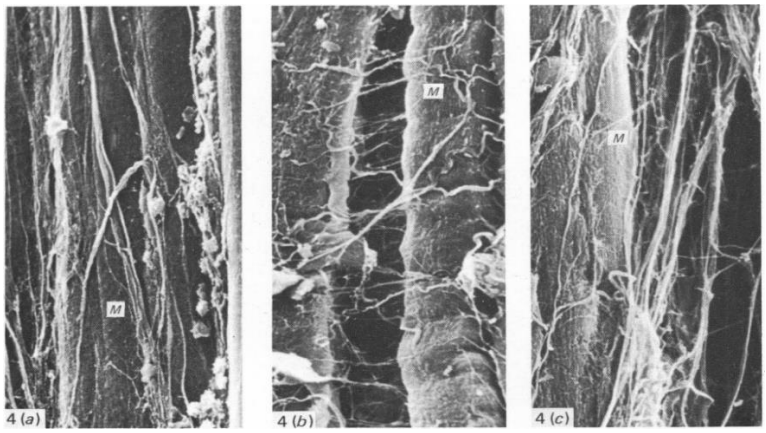

Fig.7 Scanning of collagen fibers in the perimysium; (a) normal muscle fixed in the lengthened position;(b) normal muscle fixed in the shortened position;(c) immobilized for two weeks in the shortened position; (M) muscle fiber.

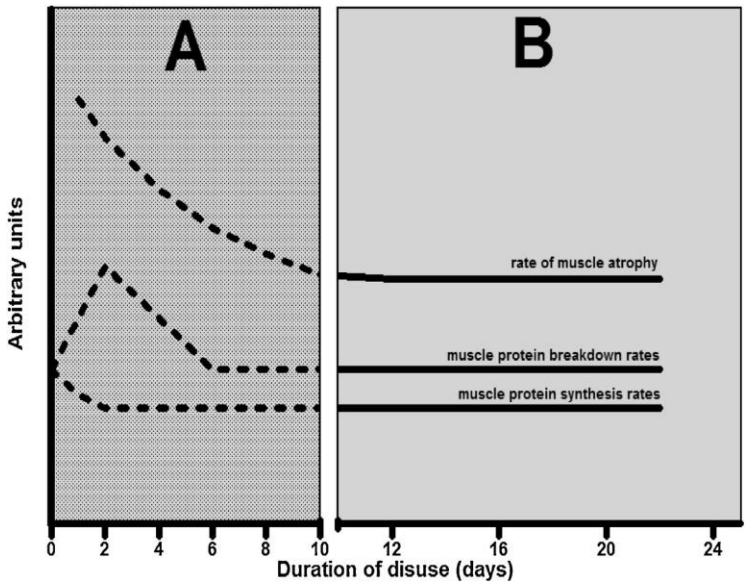

Fig.8 B.T Wall et al./Ageing research reviews[31], Theoretical schematic of the likely time of skeletal muscle atrophy during disuse, and the associated alterations of muscle protein turnover. Prior to day 0, muscle protein synthesis and breakdown rates are in balance and therefore no change in muscle mass occurs. Section A depicts the hypothesis obtained from indirect data that the onset of disuse 0-10 days leads to an increase in muscle protein breakdown rates concurrently with a decline in muscle protein synthesis rates, resulting in rapid muscle atrophy. Section B illustrates the more robust evidence available that prolonged disuse >10 days results in muscle protein breakdown rates more comparable with baseline levels, whereas muscle protein synthesis rates remain suppressed, thus facilitating a more modest rate of muscle atrophy.

Tendon

Researches from the University of Iowa stated that immobilization has a significant detrimental effect on the bone-tendon complex. They found out that after 2 weeks, a significant decrease in the mechanical properties of the native tendon appeared, but the immobilized native tendon remained significantly stronger than the repaired and immobilized one. In 4 weeks of immobilization there was a loss of strength of the bone-tendon complex in the native tendon, such that it was significantly weaker than the repaired and immobilized one. This study is important for surgeons who manage patients with immobilization and should be aware of the changes at the bone-tendon complex.[32]

Concerning the research conducted by Hokkaido University Graduate School of Medicine – they found that complete stress deprivation/immobilization of the patellar tendon induces fibroblast apoptosis (the death of cells) and that produced reparative collagen in tendons within 24 hours of casting.[33] In some cases, the tendon or the accompanying joint is immobilized for a period of days followed by an analysis of the effect on the tissues for biomechanical, biochemical and histological changes. The collagen fibrils were not uniformly oriented longitudinally with a long axis of the typical collagen fibers as in a tissue which was not been injured or undergone surgery. In other case fibrils became shortened, assembled in patches, oriented at diverse angels. Investigators have also noted a wider range of collagen fiber diameters in post-immobilized tissue.[34, 35]

Conclusion

In summary, the prolonged immobilization can cause irreversible changes in the musculoskeletal system accompanied by impaired motor function, chronic pain and more or less a predisposition for secondary trauma. Despite the above-mentioned evidence, the final decision for immobilization remains the sole discretion of the treating physician.In a clinical setting, immobility causes degeneration and alters the mechanical properties of musculoskeletal system. The increased stiffness after immobilization could be a result from quantitative and

qualitative changes in the connective tissue. All situations leading to immobilization can cause certain degree of degenerative changes in the musculoskeletal system. When immobilization is necessary, no matter the cause, every attempt should be made to minimize the duration and to address the adverse effects. Early mobilization, traction, and continuous passive motion can overcome the harmful effects of immobilization, but more research on this subject is required.

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