Chronic exposure to actual and simulated microgravity is known to lead to muscle wasting and weakness. Some information on the time course of these events may be obtained from cross sectional studies, but detailed information from longitudinal investigations is missing. Therefore the aim of the present study was to establish the rate of the structural and functional changes elicited by unilateral lower limb suspension (ULLS). The validity of this model as a paradigm of chronic disuse simulating microgravity has been demonstrated by Hather et al (1). In the present study, eight subjects (age 19.0 ± 0.2 yrs, height 1.8 ± 0.2 m, and mass 70.3 ± 2.1 kg, mean ± SE) underwent a period of 23 days of ULLS. Outcome measures obtained on days 14 and 23 of ULLS, included plantarflexion maximal voluntary contraction, triceps surae muscle volume, gastrocnemius lateralis (GL) muscle architecture, and electromyographic (EMG) activity of the soleus (SOL) and GL muscles. Physiological cross sectional area (PCSA) of the GL muscle was calculated at rest and used to estimate the intrinsic muscle force (GL force/PCSA). After 14 day of ULLS, both MVC and EMG (pooled GL+SOL) decreased (P<0.05) by 10% and 19%, respectively but plateaued thereafter. The volume of SOL, gastrocnemius medialis (GM) and GL muscles decreased (P<0.05) by 5, 6 and 5%, respectively, on day 14, and by 7 (SOL), 10 (GM) and 6% (GL) on day 23. Pennation angle and fascicle length were significantly lowered by 3 and 2% (P<0.05), respectively, on day 14. These reductions reached the level of 5 and 4% (P<0.05), respectively, on day 23. Consequently, PCSA declined by 3% (P<0.05) on day 14. As a result of the relative higher reduction of fascicle length than muscle volume between the intermediate and last measurements, PCSA did not further decrease on day 23. Similarly, the 7% (P<0.05) loss in GL force/PCSA observed on day 14 was maintained until the end of unloading period. While pennation angle and fascicle length decreased gradually throughout the intervention, it is noteworthy that the decrease in PCSA and in intrinsic force slowed down or plateaued after 14 days. These results suggest that unloading alters the intrinsic force-producing properties of the muscle at a slower rate than that predicted by atrophy alone. Further, the observed differential time course of the structural changes over the investigated period indicates that most of the adaptations induced by ULLS occur within the first 3 weeks. Lastly, the observation that after 14 days of ULLS, muscle volume kept decreasing while PCSA reached a plateau, suggests that muscle power is more compromised than strength with chronic unloading.