Fescue toxicosis results from intake of toxins in fescue containing an endophytic fungus, *Neotyphodium coenophialum*. Time-related changes in rats associated with intake of an endophyte-infected fescue diet (E+) were evaluated under thermoneutral (TN), and both short- and long-term heat stress (HS) conditions. Short-term E+ intake decreased feed intake and growth rate under both conditions, whereas rats exhibited signs of adaptation during long-term exposure with better recovery occurring under TN conditions. Rats fed an E+ diet did not change core temperature during TN, but under HS conditions they exhibited a short-term increase in core temperature above control level. However, there was adaptive return of this temperature to TN level with long-term exposure. Short-term E+ intake at TN decreased serum glucose, urea nitrogen, alkaline phosphatase, and cholesterol; whereas long-term E+ intake under these conditions resulted in complete adaptation. In contrast, short-term E+ intake at HS did not affect serum biochemistry, while long-term intake decreased all the above mentioned serum parameters. Serum prolactin level was decreased during both short- or long-term TN and HS conditions. The E+ diet decreased hepatic antioxidant gene expression, with even greater reduction as a result of HS. Long-term E+ intake and HS increased expression of cytochrome P450 and detoxification pathways, respectively. Genes associated with immune response increased with long-term E+ at TN, but decreased with E+ diet at HS. Similarly, genes coding for chaperone and DNA repair decreased with long-term E+ at TN, but increased with E+ and HS. Recovery observed in E+ rats at TN could be attributed to increased gene expression for detoxification and immune response, whereas decreased antioxidant and immune response associated genes could contribute to distress associated with E+ at HS.