The Immune Response to Resistance Exercise

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ABSTRACT

The immune response to exercise has received increased attention in the last decade. Most of this attention has focused on aerobic exercise (AEX), whereas the effect of resistance exercise (REX) has received comparatively little notice. Resistance exercise and AEX have different physiologic impacts; perhaps this also applies to the immune system. The purpose of this review was to determine a consensus from the REX immune studies that have been completed. This is complicated by the multitude of immune parameters, the varying methods used to assess them, and the paucity of studies performed. Thus, it is difficult to make a blanket statement. There is a REX-induced leukocytosis. Resistance conditioning (RCO) does not alter this response or affect the resting immune system. From these data, it appears that neither REX nor RCO demonstrates a significant impact on peripheral immunosurveillance.

Key Words: leukocytes, leukocyte subpopulations, leukocyte activation, cytokines, resistance conditioning


Introduction

Recently, the effect of physical activity on immune function has been studied intensely; the number of studies in this arena has quadrupled in the last 10 years (25). This is an important area of study because exercise may modulate the immune system’s ability to monitor and protect the individual from disease and to repair damage. In most of these studies, aerobic exercise (AEX) and aerobic conditioning (ACO) have been the independent variables. Consequently, the functional immune response to ACO seems relatively clear: a J-curve suggests that moderate levels of long-term ACO provide some protection against infectious episodes, whereas severe levels of long-term ACO seem to increase the incidence of infection above that of sedentary individuals (25, 26).

However, the immune response to resistance exercise (REX) is not as clear because fewer than a dozen studies have been published (4, 13, 15, 29). The immune response to REX may be different than that to AEX because of the different physiological demands of these 2 types of exercise. Resistance conditioning (RCO) does not have a significant effect on heart rate, blood pressure, cardiac output, stroke volume, vascular resistance, or the arteriovenous oxygen saturation difference during submaximal treadmill exercise (1, 17). Maximal oxygen uptake, heart rate, cardiac output, and blood lactate concentration are also unchanged by RCO (1, 14, 17). Peak heart rates, mean heart rates, blood lipid levels, blood lactate levels, and blood glucose levels achieved during REX do not typically reach the same levels as that during moderate-to-heavy AEX (1, 14, 20), whereas blood pressure increases to a significantly greater level than that seen during AEX (22). Additionally, REX uses primarily the phosphagen and fast glycolysis systems for energy production, whereas AEX uses slow glycolysis and aerobic pathways (20). Fast-twitch muscle fibers are recruited to a greater degree during REX (12, 23). The secretion rates and actions of hormones released during REX are also different that those released during AEX (16, 21). Thus, because of these differences, the purpose of this review is to discuss the immune response to REX, omitting cross-training studies where the REX response cannot be isolated.

A brief review of the immune system may be beneficial. The purpose of the immune system is to survey the internal environment and to identify injuries to the organism and foreign materials within the body. In either case, the immune system mounts a response to correct the situation and repair any resulting damage. Foreign objects, internal malfunctions, or even the normal activities of daily living can all cause enough harm to induce an immune response. Unlike the respiratory or cardiovascular systems, the immune system is made up of a few diffuse organs (i.e., nodes) and many unconstrained cells dispersed throughout the body. There are 5 immune cell types within the human immune system: basophils, eosinophils, lymphocytes, monocytes, and neutrophils. Lymphocytes are cells with membrane-bound receptors that react with an antigen (8) or foreign or altered object: bacteria, viruses, or damaged cells. Each lymphocyte re-
Table 1. Studies of the immune response to short-term resistance exercise by unconditioned subjects.*

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Mean ± SE age (y)</th>
<th>General exercises</th>
<th>Duration (sets × repetitions)</th>
<th>Intensity (% 1RM)</th>
<th>Immune parameters assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDowell et al. (24)</td>
<td>9 Male subjects</td>
<td>20.0 ± 0.33</td>
<td>4 Leg, 1 trunk, upper body</td>
<td>1 × 10</td>
<td>60–70</td>
<td>IgA</td>
</tr>
<tr>
<td>Simonson (32)</td>
<td>2 Groups of 8 male subjects†</td>
<td>30.2 ± 1.7</td>
<td>3 Leg, 1 trunk, 4 upper body</td>
<td>3 × 8–10</td>
<td>75</td>
<td>WBC, BA, %BA, EO, %EO, LY (CD4⁺, CD8⁺, CD4⁺/CD8⁺, NK), %LY, MO, %MO, NE, %NE</td>
</tr>
</tbody>
</table>

* 1RM = 1 repetition maximum; IgA = immunoglobulin A; WBC = white blood cell count; BA = basophil count; %BA = percentage of basophils; EO = eosinophil count; %EO = percentage of eosinophils; LY = lymphocyte count; NK = natural killer cells; %LY = percentage of lymphocytes; MO = monocyte count; %MO = percentage of monocytes; NE = neutrophil count; %NE = percentage of neutrophils.
† Control group included in study.

Short-term REX by Resistance-Conditioned Subjects

The immune response to a short-term bout of REX by resistance-conditioned individuals (Table 2) appears to be the same as that from unconditioned individuals: a generalized leukocytosis (70–80%) immediately after REX (28, 32). All major cell subpopulations, except basophils, participated in this leukocytosis (eosinophils, 40–86%; lymphocytes, 97–101%; monocytes, 90–100%; and neutrophils, 50–65%) (28, 32). Because the lymphocyte subpopulations demonstrated the same increase as the generalized WBC population, the CD4⁺/CD8⁺ ratio was unchanged as were the eosinophil and basophil counts (32).

McDowell (18) found no change in salivary IgA in response to a bout of REX by unconditioned subjects.

Short-term REX in Unconditioned Subjects

The acute immune cell response to REX in previously unconditioned subjects (Table 1) is a generalized leukocytosis (32). The leukocyte (white blood cell [WBC]) count increases (66%) immediately after REX then declines to 15% above the pre-exercise level within 30 minutes of recovery; the monocytes (88–13%) and neutrophils (47–14%) exhibit this same trend (32). The lymphocytes and the subsets CD4⁺, CD8⁺, and NK cells also demonstrate an increase (101, 80, 92, and 113%, respectively), but return to pre-exercise levels by 30 minutes of recovery (32). The greater responsiveness of the NK cells to exercise has been observed in AEX immunology studies and has been hypothesized to be due to a greater sensitivity of the NK cells to exercise-induced increases in epinephrine (2, 33). The CD4⁺/CD8⁺ ratio was unchanged as were the eosinophil and basophil counts (32).

The NK cell activity per cell was decreased (61%) after a bout of REX by resistance-conditioned individuals, and total NK cell activity was reduced (approximately 40%) due to the increase in circulating NK cells (28). The lymphocyte proliferative response, per T cell, to the mitogen concanavalin-A was unaltered (28).
**Resting Immune Status of Resistance-Conditioned Subjects**

There does not appear to be an alteration in resting immune function because of RCO (3, 24, 30–32, 34), shown in Table 3. The total WBC and the 5 WBC subpopulation (basophils, eosinophils, lymphocytes, monocytes, and neutrophils) resting numbers, ratios, and percentages of populations did not change as a result of RCO (32, 34) nor did the resting lymphocytes subsets (B, T, CD4+, percentage of CD4+, naive CD4+, % naive CD4+, memory CD4+, percentage of memory CD4+, CD8+, percentage of CD8+, suppressor CD8+, percentage of suppressor CD8+, CD4+/CD8+ ratio, and NK cells) (3, 31, 32, 34). One investigator did report a decreased percentage of T-cell (6%) and CD4+ cell counts (15%) in middle-aged men as a result of 4 weeks of anaerobic training (34). However, there are 2 treatment conditions that set this study apart from the others; it incorporated 1 hour of intense interval training (running) each week and the resistance training routine was unorthodox, 3 sets of the maximum number of repetitions possible for 1 minute at 20% of the 1 repetition maximum for 4 arm exercises (not specified) (34).

Not only are the cell numbers unchanged, but their activation levels are also not altered (30, 31). Macrophage cytokine production (tumor necrosis factor α, interleukin 1β [IL-1β], IL-1Ra, IL-2, IL-6, and prostaglandin E2) was not altered by 12 weeks of RCO (16, 30, 31). Lymphocyte proliferative responses to the mitogens phytohemagglutinin and concanavalin-A were also unchanged (31). Delayed-type hypersensitivity (induration diameter and number of positive responses) did not change either because of 12 weeks of RCO (31).

The impact of RCO on the potentially compromised immune system of older individuals is also of concern (3, 30, 31). The response of elderly patients to RCO was not different from that of young patients (30, 31).

There appears to be no resting immunoglobulin response to RCO. McDowell et al. (24) found no change in IgA levels in response to 10 weeks of RCO.

**Resting Immune Status of Long-term Resistance-Conditioned Subjects**

Long-term RCO (for a period of years) also does not alter resting immune parameters (5, 27). Calabrese et al. (5) surveyed competitive bodybuilders using and not using steroids (mean ± SD years lifting for bodybuilders using steroids, 10.62 ± 6.46; n = 13; mean ± SD years lifting for bodybuilders not using steroids, 6.55 ± 3.36; n = 11). Nieman et al. (27) studied steroid-free men who had undergone RCO for at least 3 years and were able to parallel squat at least 150% of their body weight (mean ± SE years lifting, 8.7 ± 1.1; n = 10), shown in Table 4. Immune cell numbers and percentages of populations (total WBC count, percentage of neutrophils, percentage of monocytes, number of lymphocytes, percentage of lymphocytes, number of T cells, number of activated T cells, CD4+ cell count, CD8+ cell count, and percentage of NK cells) were not different between the experienced lifters and sedentary controls (5, 27).

There appears to be no resting immunoglobulin response to long-term RCO. Concentrations of the anti-
Table 3. Studies of the resting immune status of resistance-conditioned subjects.*

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Mean ± SE age (y)</th>
<th>Program duration (wk)</th>
<th>Frequency (sessions/wk)</th>
<th>General exercises</th>
<th>Duration (sets × repetitions)</th>
<th>Intensity (% 1RM)</th>
<th>Immune parameters assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bermon et al. (3)</td>
<td>2 Groups of female subjects‡</td>
<td>71.0 ± 1.0</td>
<td>8</td>
<td>3</td>
<td>2 Leg, 1 upper body</td>
<td>3 × 8</td>
<td>80‡</td>
<td>B cells, T cells (CD4⁺, CD8⁺, CD4⁺/CD8⁺), NK cells</td>
</tr>
<tr>
<td>Horne et al. (16)</td>
<td>1 Group of 4 and 1 group of 5 female subjects‡</td>
<td>22.3 ± 3.3</td>
<td>12</td>
<td>3</td>
<td>4 Leg, 4 upper body</td>
<td>= 4 × 7</td>
<td>= 75‡</td>
<td>TNF-α</td>
</tr>
<tr>
<td>McDowell et al. (24)</td>
<td>9 Male subjects</td>
<td>20.0 ± 0.33</td>
<td>10</td>
<td>3 (2 per body part)</td>
<td>6 per session split routine</td>
<td>3 × 10 (5 wk)</td>
<td>6 × 10 (1 wk)</td>
<td>60–70‡</td>
</tr>
<tr>
<td>Rall et al. (30, 31)</td>
<td>8 Mixed</td>
<td>25.0 ± 0.7</td>
<td>12</td>
<td>2</td>
<td>2 Leg, 2 trunk, 1 upper body</td>
<td>3 × 8</td>
<td>80‡</td>
<td>B cells, T cells (CD4⁺, CD8⁺, CD4⁺/CD8⁺), Lymphocyte proliferative response to concanavalin-A, Lymphocyte proliferative response to phytohemagglutinin, IL-1Ra, IL-2, IL-6, PGE₂, IL-1Ra, DTH, DTH⁺</td>
</tr>
<tr>
<td>Simonson (32)</td>
<td>2 Groups of 8 male subjects‡</td>
<td>30.2 ± 1.7</td>
<td>6</td>
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<td>3 Leg, 1 trunk, 4 upper body</td>
<td>3 × 8–10</td>
<td>75‡</td>
<td>WBC, BA, %BA, EO, %EO, Lymphocyte proliferative response to concanavalin-A, Lymphocyte proliferative response to phytohemagglutinin, IL-1Ra, IL-2, IL-6, PGE₂, IL-1Ra, DTH, DTH⁺</td>
</tr>
<tr>
<td>Weiss et al.§ (34)</td>
<td>13 Male subjects</td>
<td>49.4 ± 1.9</td>
<td>4</td>
<td>2</td>
<td>4 Arm</td>
<td>3 × 1 min</td>
<td>20</td>
<td>Lymphocyte proliferative response to concanavalin-A, Lymphocyte proliferative response to phytohemagglutinin, IL-1Ra, IL-2, IL-6, PGE₂, IL-1Ra, DTH, DTH⁺</td>
</tr>
</tbody>
</table>

* 1RM = 1 repetition maximum; NK = natural killer; TNF-α = tumor necrosis factor α; IgA = immunoglobulin A; LY-ConA = lymphocyte proliferative response to concanavalin-A; LY-PHA = lymphocyte proliferative response to phytohemagglutinin; IL-1Ra = Interleukin-1 receptor antagonist; PGE₂ = prostaglandin E₂; DTH = ; WBC = white blood cell count; BA = basophil count; % BA = percentage of basophils; EO = eosinophil count; %EO = percentage of eosinophils; LY = lymphocyte count; %LY = percentage of lymphocytes; MO = monocyte count; %MO = percentage of monocytes; NE = neutrophil count; %NE = percentage of neutrophils.

‡ Control group included in study.

§ Intensity was progressively increased.

§ Included 1 day per week of sprint interval training.
The CD4 function as a result of RCO (3, 5, 10, 24, 27, 30–32, 34).

There also do not appear to be any long-term alterations in immune cell numbers or immune system surveil lance (19), is unchanged (3, 31, 32, 34).

Perhaps an immunochallenge administered during a conditioning program, such as an allergy or delayed-type hypersensitivity test (31), is the best method currently available. If so, REX and RCO appear to have no long-term effect on immune function in both young and old populations (30, 31).

The study by Calabrese et al. (5) of bodybuilders

bodies IgA, IgG, and IgM were unaltered by body-building (5); however, steroid use did decrease IgA (35%) and IgM (33%) levels (5). The IgA level measured in 4 of 13 steroid-using bodybuilders was subclinical (5).

Long-term RCO may enhance some cell activation levels (5) but not others (5, 27). Bodybuilders’ (steroid and nonsteroid using) lymphocyte proliferative responses to the mitogens pokeweed, phytohemagglutinin, and concanavalin-A were not different from sedentary controls; however, the Staphylococcus aureus response of bodybuilders using steroids was greater (6%) than for controls (5). The NK cell activity was unchanged for those not using steroids (5, 27) but was increased (approximately 124%) in bodybuilders using steroids (5).

Discussion

The results of these studies indicate that a short-term bout of REX causes similar WBC perturbations as a bout of high-intensity endurance (aerobic) exercise, i.e., a generalized leukocytosis with the lymphocytes and neutrophils making the greatest contribution (28, 32). The cause of the REX-associated leukocytosis could also be a strong activation of the sympathetic nervous system, which would then increase the adrenergic receptors on lymphocytes, thus causing a spilling of the lymphocytes into the circulation (28). The release of filament fragments from the working muscle might play a role in the REX-induced leukocytosis as well (28).

Immune system responses to REX and RCO should be viewed with caution, since there are many confounding variables. There is a significant amount of individual variability in the response to REX and RCO (24, 31, 32). The immune system is highly reactive to the individual’s nutritional status, stress level, seasonal variation, and current level of immunochallenge, and these immunomodulators may have a greater impact than the exercise bout (6, 31). Of the 10 studies reviewed herein, 5 used sedentary controls (3, 27, 30–32). Ideally, a conditioning study should have dietary control and periodic stress assessments. Control groups receiving no intervention, those undergoing just the RCO, and those following just the diet ought to be included as well.

Surveys of the peripheral immune system are valuable and instructive; however, the real question is whether REX improves the participant’s resistance to infectious episodes? This is a difficult response to assess. For example, although resistance to upper respiratory tract infections appears to be improved in moderately aerobically conditioned individuals, the mechanisms for this have not been identified (26).
sustained the idea that anabolic androgenic steroid use can suppress the immune system. They found that although the B cells were capable of proliferating, this did not translate into increased antibody production (5). Increased NK cell cytotoxic activity may be advantageous or injurious in that it may result in increased systemic monitoring and improved resistance to infection or to a level of surveillance that may lead to autoimmune disorders (5).

Conclusions

From these data, it appears that neither REX nor RCO demonstrates a significant impact on peripheral immunosurveillance.

Longitudinal training studies of 6 months or more would be illuminating since different responses to conditioning exercises occur in experienced weight trainers. Not only should immune cell numbers and activation levels be assessed, but in vitro function and resistance to infectious episodes should also be determined.

Practical Applications

Short-term REX does not appear to affect immunosurveillance. There also does not seem to be a long-term impact of RCO on immune function. Thus, those participating in REX or RCO should not experience an increased incidence of infectious episodes. Because REX does not negatively affect immune function, it may also be appropriate for those with compromised immune systems (DiGeorge syndrome, human immunodeficiency virus, multiple sclerosis, rheumatoid arthritis).

References


