Magnitude and Timing of the Postprandial Inflammatory Response to a High-Fat Meal in Healthy Adults: A Systematic Review

Sam R Emerson, Stephanie P Kurti, Craig A Harms, Mark D Haub, Tonatiuh Melgarejo, Cindy Logan, and Sara K Rosenkranz

ABSTRACT

Research findings over the past several decades have shown that inflammation is a prominent feature of many chronic diseases, with poor diet being one likely inflammatory stimulus. Specifically, a single high-fat meal (HFM) has been suggested to increase inflammation, although there is currently no consensus with regard to the specific changes in many of the proinflammatory markers that are frequently assessed after an HFM. The aim of this systematic review was to objectively describe the postprandial timing and magnitude of changes in 5 common inflammatory markers: interleukin (IL) 6, C-reactive protein (CRP), tumor necrosis factor (TNF)-α, IL-1β, and IL-8. Ten relevant databases were searched, yielding 494 results, of which 47 articles met the pre-established inclusion criteria: 1) healthy men and women aged 18–60 y, 2) consuming a single HFM (≥30% fat, ≥500 kcal), and 3) assessing relevant inflammatory markers postmeal for ≥2 h. The only marker found to consistently change in the postprandial period was IL-6: on average, from a baseline of 1.4 pg/mL, it peaked at 2.9 pg/mL 6 h post-HFM (an average relative change of 100%). CRP, TNF-α, IL-1β, and IL-8 did not change significantly in 79% (23 of 29), 68% (19 of 28), 67% (2 of 3), and 75% (3 of 4) of included studies, respectively. We conclude that there is strong evidence that CRP and TNF-α are not responsive at the usual time scale observed in postprandial studies in healthy humans younger than age 60 y. However, future research should further investigate the role of IL-6 in the postprandial period, because it routinely increases even in healthy participants. We assert that the findings of this systematic review on markers of inflammation in the postprandial period will considerably aid in informing future research and advancing clinical knowledge.

Introduction

Cardiovascular disease (CVD) is widely recognized to be the leading cause of death in the United States and throughout Western society. Lifestyle factors that appear to increase the risk of CVD include insufficient physical activity, obesity, and poor dietary habits. Although the causal factors leading to the manifestation of CVD are certainly complex and numerous, it has become clear that a common feature of heart and vascular diseases is inflammation. Atherosclerotic lesions, a prominent feature of CVD, are a hotbed of inflammatory activity. Briefly, immune cells such as T cells, macrophages, and mast cells will infiltrate into an atheromatous lesion, where they can perform the following: 1) promote prothrombotic factors, 2) cause the release of metalloproteinases and cysteine proteases that can reduce the stability of the atherosclerotic plaque, and 3) promote the release of proinflammatory cytokines, such as IL-6 and TNF-α. These acute markers of inflammation then travel to the liver, whereby they stimulate the increased release of chronic, low-grade markers of inflammation, such as C-reactive protein (CRP). Excessive inflammation is positively associated with type 2 diabetes, obesity, and coronary artery disease.

But what are the stimuli that jumpstart the deleterious inflammatory cascade? A commonly suggested inflammatory...
stimulus is a chronic high-fat diet. Indeed, when rodents are fed a high-fat diet, there is an increase in markers of inflammation both in adipose tissue and in the systemic vasculature (9–11). Thus, a diet high in fat and overall energy may partly cause the elevated systemic inflammation that underpins CVD, as well as insulin resistance, and is associated with obesity (12). However, the effect of dietary consumption on inflammation may not be limited to chronic intake but may be evident after the consumption of a single meal.

To this end, numerous studies have been undertaken to investigate the effects of a single high-fat meal (HFM) on postprandial inflammation (see Table 1, Supplemental Tables 1–4). Many studies have found a significant increase in markers of systemic inflammation after an HFM, whereas others have found no changes. Study design variables that could potentially affect relevant findings and consequently precipitate inter-investigation differences include meal size, meal composition, subject characteristics, previous acute exercise, postprandial period assessment length, and method of drawing blood. As a result, we are currently far from consensus with regard to the response features (i.e., timing and magnitude) after an HFM of even the most commonly assessed markers of inflammation. A synthesis of previous research that investigated postprandial inflammation, with particular attention to the specific features of the response, would inform future research and advance clinical understanding.

Therefore, the purpose of this systematic review was to characterize the postprandial inflammatory response, in terms of magnitude and timing, to an HFM in healthy men and women (aged 18–60 y) on the basis of the consolidated findings of previous relevant investigations. The markers of inflammation included in the present review include IL-6, IL-1β, IL-8, TNF-α, and CRP, because these are frequently assessed inflammatory markers in the postprandial period.

Methods

Inclusion criteria. To be incorporated into the present systematic review, there were multiple inclusion criteria that each study was required to meet. Individuals being assessed had to be men or women aged 18–60 y. Participants had to be healthy and not diagnosed with any chronic disease. Studies featuring overweight and obese participants were included in the analyses as long as they did not present with any other chronic disease. The study must have included an HFM challenge that provided ≥500 kcal of energy with ≥30% of the energy from fat. The study needed to feature a single meal or studies with serial meals provided in the postprandial period were included if there were data included for time points before the second meal. Any data reported after a second meal were excluded from the present analyses. If a study contained multiple meal trials or subsets of participants, each meal or participant group that met the inclusion criteria was considered separately. If a study included an exercise session, only the control (no exercise) condition was included. To be included, each study must have assessed ≥1 of the previously stated markers of inflammation (IL-6, IL-1β, IL-8, TNF-α, and CRP), both at baseline (fasting) and in the postprandial period for ≥2 h. Only data from full-text, peer-reviewed, and published articles were included (i.e., data from conference proceedings, abstracts, and textbooks were not included). There were no restrictions on year of publication, but only English-language articles were included. If a study did not satisfy all of the aforementioned criteria, it was excluded from the present systematic review.

Search strategy. Article searches occurred in January and February of 2016. Automatic searches were conducted weekly through manuscript preparation in order to capture very recent publications. However, recurring automatic searches produced no new articles. Databases that were searched included the following: NCBI Pubmed, Scopus, Proquest Nursing and Allied Health, Web of Science, Cochrane Library, SpringerLink, SPORTdiscus, Health and Wellness Resource Center, Health Reference Center Academic, and PsycINFO. Key search terms were as follows: “postprandial” or “post prandial;” “high fat meal,” “inflammation” or “cytokine or interleukin,” “healthy” or “normal;” and “humans” or “men” or “women.” Appropriate search modifiers were used to exclude “children,” “elder,” “rodents,” “rats,” and “mice.” Articles retrieved during searching were imported into and cataloged by using RefWorks reference management software (ProQuest LLC). The process and results of the systematic search are shown in Figure 1. There were 494 total citation hits from all databases combined. Of these, 163 citations were eliminated as duplicates (75 duplicates were retained). Of the 331 citations that passed the duplicate check, 103 citations were eliminated on the grounds of not being full-text, peer-reviewed research articles. The remaining 228 articles were assessed on the basis of the aforementioned inclusion criteria, in abstract-form only, by 2 independent reviewers (SRE and SPK). The reviewers then met to discuss the inclusion or exclusion of each abstract, and 156 articles were eliminated. Of the eliminated articles, 88 articles were eliminated due to not being postprandial studies assessing responses to a meal. The other 68 abstracts that were postprandial studies were eliminated due to not testing humans aged 18–60 y (8 articles), participants presenting with a chronic disease (12 articles), not using test meals (14 articles), or using a HFM (2 articles). The other 68 abstracts that were postprandial studies were eliminated due to not testing humans aged 18–60 y (8 articles), participants presenting with a chronic disease (12 articles), not using test meals (14 articles), or using a HFM (2 articles). The remaining 72 articles were retrieved in full-text form and thoroughly assessed by both reviewers. Finally, 25 articles were eliminated after full-text assessment, leaving 47 articles to be included in the final analyses. The reasons for the eliminated 25 full-text articles are detailed in Figure 1. Some abstracts and full-text articles were eliminated for not complying with multiple inclusion criteria.

Data extraction. Information with regard to the test meal (composition and fat and energy content), participants (number of participants, male-to-female ratio, and age and BMI of participants), blood draw method (cannula or repeated venipuncture), and length of postprandial assessment was extracted from each study. In addition, for each inflammatory marker of interest (IL-6, IL-8, IL-1β, TNF-α, and CRP), the following information was extracted: whether or not the marker significantly changed from baseline, the fasting value, the time to peak or nadir (if applicable), and the peak or nadir value (if applicable). For many studies, all of the necessary information was not explicitly included in the article. In these cases, authors were directly contacted to obtain the missing information. Many authors provided the missing information (see Acknowledgments), although some did not; thus, some data are missing from the present analyses.

Assessing risk of bias. A quality-appraisal or risk-of-bias assessment was conducted for all 47 articles included in the analyses. All of the included studies used the same general study design; therefore, traditional quality-appraisal assessment tools were not applicable to the present systematic review. Consequently, we developed an internal validity checklist to assess the strength of each study (Supplemental Appendix A). This tool included 9 criteria based on different components of postprandial inflammation study design: control of diet, fasting quality control, control of exercise, sample size adequacy, postprandial period length, blood draw frequency, blood draw method, normalization of test meal, and proper processing of inflammatory marker analyses. Each study was assessed against the above criteria and given a score ranging from 0 to 9. Studies were scored separately by 2 independent reviewers (SRE and SPK), after which the reviewers met to confirm a final score for each study.
<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Meal</th>
<th>Blood draw method</th>
<th>S or P</th>
<th>MO</th>
<th>Fat, kcal</th>
<th>Energy, kcal</th>
<th>n</th>
<th>M/F, n/n</th>
<th>Age, y</th>
<th>BMI, kg/m²</th>
<th>PPP, h</th>
<th>HFM response</th>
<th>TTP, h</th>
<th>Fasting¹ IL-6, pg/mL</th>
<th>Peak² IL-6, pg/mL</th>
<th>QA</th>
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<tbody>
<tr>
<td>Arjunan et al., 2013–2015</td>
<td>South Asian (13)</td>
<td>White bread, butter, cheese, milkshake</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>57</td>
<td>14.3</td>
<td>10</td>
<td>10 M/0 F</td>
<td>22.3 ± 1.3</td>
<td>254 ± 2.5</td>
<td>9 ↑</td>
<td>13.1 ± 1.11</td>
<td>3.47 ± 1.43</td>
<td>6</td>
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<tr>
<td>Arjunan et al., 2013–2015</td>
<td>European (13)</td>
<td>White bread, butter, cheese, milkshake</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>57</td>
<td>14.3</td>
<td>10</td>
<td>10 M/0 F</td>
<td>23.2 ± 2.0</td>
<td>252 ± 1.6</td>
<td>9 ↑</td>
<td>1.25 ± 0.80</td>
<td>2.65 ± 1.40</td>
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<tr>
<td>Arjunan et al., 2015–2015</td>
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<td>White bread, butter, cheese, milkshake</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>57</td>
<td>14.3</td>
<td>15</td>
<td>15 M/0 F</td>
<td>24.0 ± 3.0</td>
<td>254 ± 3.3</td>
<td>9 ↑</td>
<td>0.80 (050-1.28)</td>
<td>6.39 ± 6.20</td>
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<td>White bread, butter, cheese, milkshake</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>57</td>
<td>14.3</td>
<td>14</td>
<td>14 M/0 F</td>
<td>22.0 ± 1.0</td>
<td>227 ± 2.2</td>
<td>9 ↑</td>
<td>0.93 (0.50-1.95)</td>
<td>4.48 ± 4.90</td>
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<tr>
<td>Bidwell et al., 2014</td>
<td>South Asian (14)</td>
<td>Cheese, milkshake</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>40</td>
<td>600</td>
<td>22</td>
<td>11 M/11 F</td>
<td>M: 208 ± 0.7; F: 215 ± 0.7</td>
<td>M: 239 ± 0.9; F: 211 ± 0.5</td>
<td>6 ↑</td>
<td>NS</td>
<td>NS</td>
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<td>Brandauer et al., 2013</td>
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<td>Cheese, milkshake</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>46</td>
<td>852</td>
<td>25</td>
<td>13 M/12 F</td>
<td>27 ± 1</td>
<td>246 ± 0.7</td>
<td>4 ↑</td>
<td>0.64 ± 0.39</td>
<td>0.97 ± 0.64</td>
<td>45</td>
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<tr>
<td>Burton-Freeman et al., 2012</td>
<td>Australian (17)</td>
<td>Liquid test meal</td>
<td>Cannula</td>
<td>P</td>
<td>Y</td>
<td>30</td>
<td>750</td>
<td>7</td>
<td>6 M/1 F</td>
<td>23.0 (21.0-26.0)</td>
<td>203 (189-251)</td>
<td>6 ↑</td>
<td>0.61 (0.56-2.37)</td>
<td>3.69 ± 1.13</td>
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<tr>
<td>Caixàs et al., 2008</td>
<td>Lean (18)</td>
<td>Apple muffins, milkshake</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>60</td>
<td>976</td>
<td>15</td>
<td>15 M/0 F</td>
<td>28 ± 9</td>
<td>NS</td>
<td>6 ↓</td>
<td>1.6 ± 0.3</td>
<td>1.3 ± 0.3</td>
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<tr>
<td>Delgado-Lista et al., 2011</td>
<td>Turkish (20)</td>
<td>Whipping cream, fruit, cereal, nuts, chocolate</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>67</td>
<td>1075</td>
<td>8</td>
<td>8 M/0 F</td>
<td>27.8 ± 12.1</td>
<td>236 ± 1.0</td>
<td>6 ↑</td>
<td>1.34 ± 1.16</td>
<td>6.93 ± 5.77</td>
<td>5</td>
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<tr>
<td>Drew et al., 2014</td>
<td>Turkey burger, white bread</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>50</td>
<td>600</td>
<td>16</td>
<td>16 M/0 F</td>
<td>45 ± 11</td>
<td>276 ± 5.3</td>
<td>6 ↑</td>
<td>1.96 ± 1.70</td>
<td>3.35 ± 2.29</td>
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<td>Ehlers et al., 2014</td>
<td>Hamburger, French fries</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>39</td>
<td>1106</td>
<td>6</td>
<td>6 M/0 F</td>
<td>44.3 ± 5.2</td>
<td>248 ± 2.5</td>
<td>8 ↑</td>
<td>6 NS</td>
<td>NS</td>
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<tr>
<td>Esser et al., 2013</td>
<td>Milkshake (cream, sugar, water)</td>
<td>Cannula</td>
<td>P</td>
<td>Y</td>
<td>85</td>
<td>954</td>
<td>20</td>
<td>20 M/0 F</td>
<td>22 ± 2</td>
<td>227 ± 2.4</td>
<td>6 ↑</td>
<td>0.74 ± 0.24</td>
<td>1.38 ± 0.73</td>
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<td>Gill et al., 2003</td>
<td>Whipping cream, fruit, cereal, nuts, chocolate</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>67</td>
<td>1075</td>
<td>8</td>
<td>8 M/0 F</td>
<td>27.8 ± 12.1</td>
<td>236 ± 1.0</td>
<td>6 ↑</td>
<td>1.34 ± 1.16</td>
<td>6.93 ± 5.77</td>
<td>5</td>
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<td>Gregersen et al., 2012</td>
<td>Cheese, eggs, oil, cream, white bread</td>
<td>Cannula</td>
<td>P</td>
<td>Y</td>
<td>77</td>
<td>928</td>
<td>15</td>
<td>4 M/11 F</td>
<td>44 ± 3</td>
<td>263 ± 20</td>
<td>3 ↑</td>
<td>0.87 ± 0.12</td>
<td>1.13 ± 0.1</td>
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<tr>
<td>Harrison et al., 2009</td>
<td>Crossants, butter, ice cream, chocolate, potato crisps</td>
<td>Cannula</td>
<td>S</td>
<td>N</td>
<td>60</td>
<td>1450</td>
<td>8</td>
<td>8 M/0 F</td>
<td>26.9 ± 4.1</td>
<td>260 ± 3.6</td>
<td>6 ↑</td>
<td>0.74 ± 0.45</td>
<td>3.13 ± 2.87</td>
<td>55</td>
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<td>Jiménez-Gómez et al., 2009</td>
<td>Butter, whole-meal bread, hard-boiled egg, whole milk, ice cream, whipping cream</td>
<td>Venipuncture</td>
<td>P</td>
<td>Y</td>
<td>60</td>
<td>20</td>
<td>20 M/0 F</td>
<td>NS</td>
<td>NS</td>
<td>9 ↓</td>
<td>— NS</td>
<td>6</td>
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<td>Johnson et al., 2016</td>
<td>Eggs, turkey sausage, biscuits, gravy</td>
<td>Cannula</td>
<td>P</td>
<td>N</td>
<td>45</td>
<td>1360-2160</td>
<td>12</td>
<td>12 M/0 F</td>
<td>23.0 ± 3.2</td>
<td>245 ± 2.7</td>
<td>4 ↑</td>
<td>— 29.8 ± 38.0</td>
<td>—</td>
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<td>Keckol-Glaser et al., 2015</td>
<td>Eggs, turkey sausage, biscuits, gravy</td>
<td>Cannula</td>
<td>S</td>
<td>N</td>
<td>60</td>
<td>930</td>
<td>86</td>
<td>43 M/43 F</td>
<td>38.22 ± 8.18</td>
<td>3207 ± 5.83</td>
<td>7 ↑</td>
<td>1.76 ± 4.03</td>
<td>4.34 ± 3.03</td>
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(Continued)
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<th>Study (reference)</th>
<th>Meal</th>
<th>Blood draw method</th>
<th>S or P</th>
<th>MO</th>
<th>Fat $^2$</th>
<th>Energy, kcal</th>
<th>M/F, n/n</th>
<th>Age, y</th>
<th>BMI, kg/m$^2$</th>
<th>PPP, h</th>
<th>HFM response</th>
<th>TTP, h</th>
<th>Fasting$^3$ IL-6, pg/mL</th>
<th>Peak$^4$ IL-6, pg/mL</th>
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<tr>
<td>Kračmerová et al., 2014 (30)</td>
<td>Pork meat, egg, French fries, hazelnut spread, croissant</td>
<td>Cannula</td>
<td>P Y</td>
<td>47</td>
<td>1470</td>
<td>10 10 W/O F</td>
<td>26.3 ± 1.04</td>
<td>23.11 ± 0.59</td>
<td>4</td>
<td>↑</td>
<td>4</td>
<td>0.899 ± 0.509</td>
<td>2.168 ± 0.44</td>
<td>3.5</td>
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<td>Lundman et al., 2007 (31)</td>
<td>Pasta, chicken, peas, mayonnaise</td>
<td>Venipuncture</td>
<td>P Y</td>
<td>60</td>
<td>1000</td>
<td>26 26 W/O F</td>
<td>51 ± 3</td>
<td>264 ± 3.3</td>
<td>6</td>
<td>↑</td>
<td>4</td>
<td>3.81 ± 3.49</td>
<td>NS</td>
<td>65</td>
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<td>Madec et al., 2011 (32)</td>
<td>Butter, bread, ham, milk cream, sucrose, whey protein</td>
<td>Cannula</td>
<td>P Y</td>
<td>52</td>
<td>730</td>
<td>16 NS</td>
<td>NS</td>
<td>NS</td>
<td>6</td>
<td>↔</td>
<td>—</td>
<td>0.43 ± 0.27</td>
<td>—</td>
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<tr>
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<td>Fried potatoes, eggs, cheese, bread rolls</td>
<td>Cannula</td>
<td>P N</td>
<td>70</td>
<td>1200</td>
<td>10 10 W/O F</td>
<td>34 ± 9</td>
<td>302 ± 1.5</td>
<td>6</td>
<td>↔</td>
<td>—</td>
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<td>—</td>
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<td>P Y</td>
<td>52</td>
<td>1416</td>
<td>15 13 W/O F</td>
<td>45 ± 8</td>
<td>267 ± 1.9</td>
<td>8</td>
<td>↑</td>
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<td>0.3 ± 0.3</td>
<td>0.97 ± 0.52</td>
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<td>Venipuncture</td>
<td>P N</td>
<td>59</td>
<td>760</td>
<td>20 10 W/O F</td>
<td>44 ± 5</td>
<td>268 ± 1.2</td>
<td>4</td>
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<td>2</td>
<td>1.9 ± 1.0</td>
<td>3.1 ± 1.0</td>
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<td>Cannula</td>
<td>P Y</td>
<td>64</td>
<td>1600–2200</td>
<td>39 39 W/O F</td>
<td>44.0 ± 9.1</td>
<td>289 ± 4.3</td>
<td>8</td>
<td>↑</td>
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<td>2.40 ± 1.36</td>
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<td>Payette et al., 2009–women (36)</td>
<td>Cheese, eggs, toast, butter, cream, milk, peanut butter</td>
<td>Cannula</td>
<td>P Y</td>
<td>64</td>
<td>1600–2200</td>
<td>41 0 W/M/F</td>
<td>43.7 ± 9.4</td>
<td>265 ± 5.7</td>
<td>8</td>
<td>↑</td>
<td>8</td>
<td>2.77 ± 1.81</td>
<td>5.83 ± 3.49</td>
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</tr>
<tr>
<td>Peluso et al., 2012 (37)</td>
<td>Fried potatoes, eggs, cheese, bread</td>
<td>Cannula</td>
<td>P N</td>
<td>55</td>
<td>1344</td>
<td>14 12 W/O F</td>
<td>45.1 ± 8.6</td>
<td>268 ± 2.2</td>
<td>8</td>
<td>↑</td>
<td>8</td>
<td>0.39 ± 0.27</td>
<td>1.09 ± 0.20</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Phillips et al., 2013–lean (38)</td>
<td>Bacon, egg, muffin, hash browns, milk</td>
<td>Cannula</td>
<td>P N</td>
<td>52</td>
<td>989</td>
<td>10 10 W/O F</td>
<td>43.4 ± 11.3</td>
<td>228 ± 1.5</td>
<td>6</td>
<td>↑</td>
<td>6</td>
<td>0.9 ± 0.3</td>
<td>NS</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Phillips et al., 2013–obese (38)</td>
<td>Bacon, egg, muffin, hash browns, milk</td>
<td>Cannula</td>
<td>P N</td>
<td>52</td>
<td>989</td>
<td>10 10 W/O F</td>
<td>40.9 ± 9.8</td>
<td>382 ± 6.7</td>
<td>6</td>
<td>↑</td>
<td>6</td>
<td>2.0 ± 1.3</td>
<td>NS</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Poppitt et al., 2008 (39)</td>
<td>Blueberry muffin</td>
<td>Venipuncture</td>
<td>S Y</td>
<td>71</td>
<td>748</td>
<td>18 18 W/O F</td>
<td>23 ± 4</td>
<td>229 ± 2.0</td>
<td>6</td>
<td>↑</td>
<td>6</td>
<td>293 ± 16.8</td>
<td>33.4 ± 16.4</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Rankin et al., 2008 (40)</td>
<td>Eggs, sausage, biscuit, pancake, jelly candy</td>
<td>Venipuncture</td>
<td>S Y</td>
<td>53</td>
<td>900</td>
<td>17 8 W/F</td>
<td>26.5 ± 7.6</td>
<td>335 ± 6.7</td>
<td>4</td>
<td>↔</td>
<td>—</td>
<td>1.5 ± 1.1</td>
<td>—</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Sandes et al., 2011 (41)</td>
<td>Muffin, milkshake</td>
<td>Cannula</td>
<td>P N</td>
<td>53</td>
<td>846</td>
<td>50 25 W/25 F</td>
<td>254 ± 4.2; F: 242.2 ± 6.3</td>
<td>M: 23.3 ± 21; F: 237 ± 34</td>
<td>8</td>
<td>↑</td>
<td>8</td>
<td>0.4 ± 0.1</td>
<td>0.9 ± 0.2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Schmid et al., 2015 (42)</td>
<td>Bread, salami, palm fat, boiled eggs</td>
<td>Cannula</td>
<td>P Y</td>
<td>61</td>
<td>1005</td>
<td>21 21 W/O F</td>
<td>418 ± 90</td>
<td>271 ± 8.2</td>
<td>6</td>
<td>↑</td>
<td>6</td>
<td>3.0 ± 1.1</td>
<td>5.1 ± 1.9</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Schwander et al., 2014–NW (43)</td>
<td>Bread, salami, palm fat, boiled eggs</td>
<td>Cannula</td>
<td>S Y</td>
<td>61</td>
<td>1000</td>
<td>19 19 W/O F</td>
<td>40.6 ± 9.2</td>
<td>236 ± 1.4</td>
<td>6</td>
<td>↔</td>
<td>—</td>
<td>20.1 ± 1.7</td>
<td>—</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Schwander et al., 2014–obese (43)</td>
<td>Bread, salami, palm fat, boiled eggs</td>
<td>Cannula</td>
<td>S Y</td>
<td>61</td>
<td>1000</td>
<td>17 17 W/O F</td>
<td>44.1 ± 8.0</td>
<td>388 ± 4.9</td>
<td>6</td>
<td>↔</td>
<td>—</td>
<td>17.9 ± 1.7</td>
<td>—</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Schwander et al., 2014–NW (43)</td>
<td>Bread, salami, palm fat, boiled eggs</td>
<td>Cannula</td>
<td>S Y</td>
<td>61</td>
<td>1500</td>
<td>19 19 W/O F</td>
<td>40.6 ± 9.2</td>
<td>236 ± 1.4</td>
<td>6</td>
<td>↔</td>
<td>—</td>
<td>19.8 ± 1.9</td>
<td>—</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Schwander et al., 2014–obese (43)</td>
<td>Bread, salami, palm fat, boiled eggs</td>
<td>Cannula</td>
<td>S Y</td>
<td>61</td>
<td>1500</td>
<td>17 17 W/O F</td>
<td>44.1 ± 8.0</td>
<td>388 ± 4.9</td>
<td>6</td>
<td>↑</td>
<td>4</td>
<td>16.7 ± 1.5</td>
<td>21.7 ± 1.9</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Strohacker et al., 2012 (44)</td>
<td>Sausage, egg, cheese, biscuit, hash browns</td>
<td>Cannula</td>
<td>P N</td>
<td>59</td>
<td>1070</td>
<td>8 4 W/F</td>
<td>21 ± 3</td>
<td>23.1 ± 3.9</td>
<td>3</td>
<td>↔</td>
<td>—</td>
<td>1.7 ± 0.9</td>
<td>—</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

(Continued)
Statistical analyses. Data analyses were performed by using GraphPad Prism (version 6.05; GraphPad Software) and SPSS Statistics software (version 22; IBM Corporation). The primary outcome measures in this review were mean baseline and peak values and the time-to-peak value for each marker of inflammation (in some studies, certain inflammatory markers were found to decrease, in which case the nadir and time-to-nadir values were used). Fasting and peak values for each inflammatory marker were assessed for objective statistical outliers by using the robust regression and outlier removal (ROUT) method (50), which utilizes nonlinear regression, in GraphPad Prism. The Q value (or maximum false-discovery rate) was set at 1%. The ROUT method involves 3 steps. First, a robust nonlinear regression is used to fit a curve that is not affected by outliers. Second, the residuals of the robust regression are assessed to determine whether or not there are any outliers. The third step of the ROUT method is simply removing the outliers from the data set. Nine outliers (7 fasting values and 2 peak values) were removed from the IL-6 data set, 1 outlier (a fasting value) was removed from the CRP data set, and 7 outliers (4 fasting values and 3 peak values) were removed from the TNF-α data set. The data sets for IL-8 and IL-1β were too small for outlier analyses; thus, all values were retained. For analyses of changes and differences between baseline and peak values, if there was no significant change postmeal for a given marker in a study, the baseline value was used as both the fasting value and the peak value in order to have a complete data set and not bias the findings toward a significant change. Many studies did not report a post-HFM value in the event of no significant change. Thus, in the original analyses, in all studies that did not find a significant change after the meal, the baseline value was used as the postmeal value. However, a secondary analysis that included post-HFM values of studies that did not find a significant change (when available) did not appreciably change the results. In addition, the studies that did report a nonsignificant postmeal value generally did not find a biologically significant change either. A paired t test was used to assess differences between mean baseline and peak IL-6 values from each study. This analysis was only performed for IL-6 because most studies found no significant change in the other markers postmeal. Spearman rank correlations were used to assess relations between percentage change in IL-6 (from fasting to peak) and mean participant BMI, mean participant age, energy content (in kilocalories) of the test meal, and percentage of energy content from fat in the test meal. Because BMI and percentage change in IL-6 were not normally distributed, they were transformed by using the Log-10 method. Data are presented as means ± SDs. For all relevant analyses, the P value was set at < 0.05.

Results

Table 1 and Supplemental Tables 1–4 show the extracted information from each study separated by the respective marker of inflammation. Some studies are represented in multiple tables, because they assessed >1 of the relevant markers of inflammation. For IL-6, 32 of 45 studies (~71%) found a significant increase in the marker after HFM consumption. Ten studies (~22%) found no change in IL-6 post-HFM, 2 studies (~4%) found a significant decrease, and 1 study did not report whether or not the marker changed. Of the 32 studies that found a significant increase, 2 used repeated venipuncture and 30 used a cannula. In studies that found a significant change post-HFM, the time to peak was 5.9 ± 2.0 h. For 22 of the 34 studies that found a significant postprandial IL-6 change, the mean peak value occurred at the final time point assessed in the study protocol. Before the removal of outliers, the baseline (fasting) and peak IL-6 values for all studies combined were 4.83 ± 8.02 and 4.76 ± 6.87 pg/mL, respectively. After outlier removal, the mean baseline and peak values were 1.37 ± 0.93 and 2.85 ± 1.85 pg/mL, respectively. The
found a decrease, and 19 studies (~68%) found no significant change in TNF-α from baseline during the postprandial period. Before the removal of outliers, fasting and peak TNF-α values were 33.5 ± 143.5 and 102.0 ± 242.0 pg/mL, respectively. After the removal of outliers, the fasting and peak values were 2.76 ± 1.95 and 2.85 ± 2.02 pg/mL, respectively. In the studies that found a significant postmeal TNF-α increase, the peak occurred at 5.5 ± 3.0 h. In the studies that found a decrease, the nadir occurred at 7.5 ± 1.0 h. Figure 2C provides a visual representation of change or stagnation of TNF-α after HFM intake for the studies that passed the outlier check.

With regard to IL-1β, 3 studies assessed this marker in the postprandial period. Two studies found no significant change from baseline during the postprandial period, whereas 1 study found a significant decrease. In this study, the mean nadir value occurred at 4 h postmeal. Figure 2D shows fasting and postprandial values for the 3 studies that measured IL-1β.

Four studies measured IL-8 in the postprandial period. Of these, 1 study found a significant increase in IL-8 from baseline to peak and 3 studies found no change. The baseline value for IL-8 was 2.29 ± 0.36 pg/mL. In the 1 study that found a significant increase, a peak value of 3.26 ± 2.56 pg/mL was found 4 h after the HFM. Figure 2E shows the mean and individual values for IL-8 at baseline and postmeal for the 4 respective studies.

Figure 3 shows correlations of the percentage change in IL-6 from fasting to postmeal with different independent variables that could potentially affect the IL-6 response. There was a significant negative correlation (ρ = −0.42, P = 0.02) between the percentage of energy from fat in the test meal and the percentage change in IL-6 (Figure 3A). There was not a significant correlation (ρ = 0.23, P = 0.26) between the energy content of the test meal and the percentage change in IL-6 (Figure 3B). Similarly, mean BMI showed no significant relation (ρ = −0.12, P = 0.55) with the percentage change in IL-6 (Figure 3C). Finally, there was not a significant negative correlation (ρ = −0.28, P = 0.16) between mean age of the participants and the percentage change in IL-6 (Figure 3D).

The results of the quality appraisal for each study are shown in Table 1 and Supplemental Tables 1–4. There was little variability in quality-assessment scores among studies, ranging from 2.5 to 6.5 points out of a possible 9 points. Generally, no differences were observed between studies with regard to appraisal score and whether or not a postprandial inflammatory change was detected. Because the quality-appraisal scores did not noticeably affect our primary outcomes, we did not adjust analyses to weight studies differently on the basis of appraisal score. Furthermore, because the research questions primarily involved calculation of baseline and peak means in inflammatory markers (as opposed to effect sizes of interventions, etc.), the present analyses did not fit well with traditional meta-analyses statistics conducted within systematic reviews.

Figure 1 Flowchart of article search and selection process. Ten relevant databases were searched, yielding 494 total citations. The final number of citations included in the present study was 47. See Methods section for more details.

mean percentage change from baseline to peak (after outlier removal) was 153% ± 256%. After the removal of outliers, but including studies that found no change or a decrease in IL-6 post-HFM, there was a significant increase (P < 0.0001) in IL-6 from baseline to peak value. Figure 2A shows the change in IL-6 from fasting to peak values for each individual study (after outlier removal) and the mean response.

Twenty-nine studies met the inclusion criteria and measured CRP in the postprandial period. Of these, 23 studies (~79%) found no change in CRP in the assessed postprandial period. Four studies (~14%) found an increase and 2 studies (~7%) found a decrease in CRP after the meal. Of the studies that found an increase, the peak occurred at 4.7 ± 2.3 h post-HFM. The fasting values for CRP were 1.50 ± 1.15 g/L before outlier removal and 1.35 ± 0.86 g/L after outlier removal. Three of the 4 studies that found a significant increase in CRP post-HFM did not report the peak value; thus, a mean peak value was not calculated. Figure 2B shows the mean and individual responses of CRP to an HFM for all studies.

TNF-α was assessed in 28 of the included studies. Five studies (~18%) found an increase, 4 studies (~14%)
Discussion

Main findings. The purpose of this systematic review was to characterize the magnitude and timing of changes in markers of inflammation after HFM consumption with the use of methodically selected research articles that met pre-established criteria. The primary findings were as follows: 1) that, very often, there was a postprandial increase in IL-6; 2) IL-6 typically peaked at \( \sim 2.9 \) pg/mL or, more relatively, exhibited an \( \sim 100\% \) increase from baseline that typically occurred \( \sim 5.9 \) h after the HFM; 3) TNF-\( \alpha \) and CRP were assessed many times and yet very infrequently showed an increase post-HFM; 4) IL-8 and IL-1\( \beta \) have only rarely been assessed post-HFM in studies meeting our criteria; and 5) in studies that did assess IL-8 and IL-1\( \beta \), although equivocal, the data suggested that these markers of inflammation did not significantly change after the consumption of an HFM. We believe that these findings are likely to be instrumental in advancing our understanding of the immune and inflammatory status of healthy individuals before and after HFM intake and will have utility in designing and interpreting future research.

Importance of postprandial inflammation. Why should we be concerned with the timing and magnitude of inflammatory cytokine responses after HFM ingestion? It is because substantial research points to the notion that persistent low-grade inflammation is an underlying factor in several high-mortality chronic diseases and that diet can contribute to, or attenuate, that inflammation (5). It was previously thought that atherosclerosis was a lipid-storage disease (7). However, we have come to realize the vital role of inflammation in the etiology of vascular diseases (5, 6, 51). Certainly, lipids play a role in the disease process, because subendothelial penetration and retention of lipoproteins can serve as an initiating event for the atherosclerotic cascade (52). However, once the lipoproteins are in the endothelium, oxidative stress and inflammation processes assume a prominent role (6, 7). The lipoproteins are oxidized by reactive oxygen species, forming oxidized LDL. Oxidized LDL particles have several proinflammatory effects, including the following: 1) increased expression of adhesion molecules [e.g., vascular cell adhesion molecule 1 (VCAM-1) and intercellular adhesion molecule 1 (ICAM-1)], which promote the adhesion and penetration of immune cells to the endothelium (53); 2) increased proinflammatory cytokine release (54); and 3) activation of smooth muscle and endothelial cells (55). In turn, the increased presence of immune cells, via the functions of adhesion molecules, further increases the oxidation of lipoproteins (7). Many oxidized LDL particles will be phagocytically ingested by macrophages. These macrophages, formerly monocytes, are present consequent to their recruitment by inflammatory mediators, such as cytokines, and the linkage and induction properties of adhesion molecules (6). When monocytes penetrate the endothelium, they differentiate into macrophages. Macrophages play a crucial role in the inflammatory processes that characterize atherosclerosis. Macrophages present cell surface receptors, which, when activated, result in the increased production of many proinflammatory cytokines and adhesion molecules (56). Furthermore, as macrophages become increasingly lipid-laden as a result of oxidized lipoprotein phagocytosis,
they will be laid down in the endothelium as foam cells, which are the hallmark cells of the atherosclerotic process and promote the progression of intima media thickness (6).

The increased production of proinflammatory cytokines throughout the process outlined above is important considering their physiologic effects. First, cytokines act as intermediary messengers, recruiting immune cells such as monocytes, dendritic cells, and lymphocytes to the site of vascular damage and increasing the inflammatory tone of the endothelium (57). Furthermore, it appears that inflammatory cytokines promote the activation of vascular smooth muscle and increase vascular sympathetic tone. These effects are evidenced by increased systolic blood pressure, decreased flow-mediated dilation, reduced release of the vasodilator NO, and decreased nitroglycerin-induced vasodilation (58). There is also evidence that proinflammatory cytokines, such as IL-6 and TNF-α, directly increase insulin resistance in adipocytes (59). Finally, locally produced proinflammatory cytokines often travel to the liver and increase the production of acute-phase response proteins, such as CRP and serum amyloid A (SAA) (6, 12). CRP and SAA are strongly associated with chronic disease risk. Briefly, CRP concentrations have been shown to be predictive of, among other things, peripheral vascular disease (60), future cardiovascular events (61), and ischemic stroke and transient ischemic attack (62). Similarly, SAA concentrations have been shown to be associated with coronary artery disease and future cardiovascular events (63). However, evidence that implicates markers of inflammation with CVD is not limited to acute-phase response proteins. Elevated concentrations of IL-6 in circulation are associated with myocardial infarction (64), mortality (65), and type 2 diabetes (66). Evidence linking inflammatory marker concentrations to chronic disease also exists for TNF-α (67), IL-1β (68), and IL-8 (69). Clearly, there is a connection between elevated markers of systemic inflammation and the development of disease.

The connection between diet and systemic inflammatory tone has often been suggested (70, 71). Several studies have investigated potential single-meal effects on markers of inflammation, with most studies using HFMs. However, as evidenced by our findings, there is inconsistency and ambiguity between studies with regard to the “normal” inflammatory response to an HFM. A recent review (12) performed a similar systematic search (with slightly different inclusion and exclusion criteria) and compilation of findings, but the authors elected to not quantify the collective response characteristics across studies. In the context of the equivocal nature of the postprandial inflammation research findings to date, as well as considering the physiologically important implications of altered inflammatory marker concentrations, the present systematic review was conducted to better inform future research studies, as well as to advance our understanding with regard to which inflammatory markers are responsive in the transient window after HFM intake.

**Findings for individual inflammatory markers.** The present review found that the majority of studies detected an increase in IL-6 after the consumption of an HFM, which agrees with the findings of Herieka and Erridge (12). The increase is generally robust, because the average relative increase is ~100% of the baseline value; thus, IL-6 is quite

![Figure 3](image-url)
responsive to HFM intake. It has been suggested that detected increases in IL-6 in the postprandial period should be viewed with skepticism, because the process of cannulation has been shown to lead to increases in local IL-6 production (72). Indeed, it has been shown that cannulation without HFM consumption can lead to increases in IL-6 that are similar to those seen after HFM intake (73). In the present review, the vast majority of articles (30 of 32) that found a significant increase in IL-6 post-HFM used the insertion of a cannula for repeated blood sampling. Thus, it is possible that, in these studies, some or all of the increase in IL-6 could be an artifact of a local inflammatory response to the cannula, as opposed to a systemic response to the meal. However, 2 important points should be considered. First, 2 studies in our analysis used repeated venipuncture for blood sampling and found significant postprandial increases in IL-6 (35, 49). Second, one study (25) found both a significant increase in circulating IL-6 with the use of a forearm cannula and an increase in muscle expression of IL-6 with the use of a vastus lateralis biopsy, suggesting a systemic effect and not merely a local inflammatory response to the cannula. Collectively, these considerations suggest that at least some, if not all, of the IL-6 response to an HFM can be credited to the meal intake, instead of simply a local inflammatory response to cannulation. Regardless, because the majority of postprandial inflammation studies use cannulation, our findings nonetheless quantify the timing and magnitude of the collective IL-6 response to cannulation and an HFM. Because IL-6 is by far the most frequently assessed marker of inflammation in the postprandial period, and in consideration of its varied function in the progression of atherosclerosis, we assert that the findings of the present analyses have relevant clinical and research implications. Namely, elevated IL-6 concentrations have been linked to multiple clinical considerations. IL-6 concentrations have been found to be significantly associated with systolic and diastolic blood pressure, fasting insulin, and insulin sensitivity (74). A systematic review found that long-term elevated IL-6 concentrations are associated with coronary artery disease to a similar degree as most traditional risk factors (75). Finally, high IL-6 concentrations have been associated with mortality in a population-based study in older adults (65). Harris et al. (65) found that the individuals in the highest IL-6 quartile, and who therefore presented the highest mortality risk, showed IL-6 concentrations >3.19 pg/mL. Interestingly, the present review found that IL-6 starts at ~1.4 pg/mL and peaks at ~3 pg/mL after an HFM in healthy adults aged <60 y. Thus, a single HFM can induce a considerable postprandial increase in which circulating IL-6 concentrations can approach clinically high concentrations, even in young healthy individuals. Although more research is needed with regard to the clinical importance of acute IL-6 fluctuations, considering the established relations between IL-6 concentrations and adverse health outcomes, these acute IL-6 fluxes likely represent an important physiologic occurrence similar to other postprandial excursions (e.g., TGs, glucose) that have been shown to be associated with negative health outcomes.

On the basis of our search results, CRP was the second most frequently assessed (29 studies) marker of inflammation in the postprandial period after HFM intake. Because ~80% of these studies found no significant change in CRP in the assessed postprandial period, and considering that the remaining 6 studies that found a significant change were divided in their findings (i.e., 4 found a significant increase and 2 found a significant decrease), the evidence strongly suggests that CRP is not a responsive marker of inflammation in the typically assessed 4- to 8-h postprandial period in healthy adults. This assertion is in agreement with our understanding of the physiologic pathway that results in an increase in CRP. The main drivers behind an increase in circulating CRP are proinflammatory cytokines produced locally at the site of damage (e.g., the inflamed endothelium). These proinflammatory cytokines, especially IL-6, then travel to the liver and stimulate increased production of acute-phase response proteins, such as CRP and SAA (6). The time course by which this pathway occurs is considerably slower than those of locally produced cytokines, because there is typically no detectable change in the first 5 h after a stimulus. Instead, CRP will slowly increase and peak at ~24 h poststimulus. [Note: these responses are typically experimentally described by using an endotoxin model, not necessarily an HFM (12).] Thus, because CRP and other acute-phase response proteins reflect the cumulative inflammatory response (i.e., include the amplification and stimulation of many locally produced inflammatory molecules and their subsequent stimulation of acute-phase response proteins in the liver), as well as bearing in mind the delayed increase and decrease in acute-response phase proteins, CRP is a particularly advantageous marker of chronic inflammation to assess both clinically and in research. However, for these same reasons, CRP is not a viable inflammatory marker to assess in a prototypical postprandial assessment study. In consideration of the delayed response of CRP poststimulus, in combination with the findings of the present review indicating that CRP shows no change in the vast majority of postprandial inflammation studies, we recommend that CRP no longer be assessed for postprandial changes in response to an HFM in healthy adults. To be sure, CRP retains its utility in assessing overall or baseline inflammatory status; however, it is simply unlikely to change in the 4-8 h after the ingestion of an HFM in healthy individuals <60 y of age.

TNF-α has also been widely assessed in the postprandial period as an inflammatory marker that is thought to typically increase after HFM intake. Specifically, TNF-α, like IL-6, is believed to increase quickly in the poststimulus period, peaking at ~2–3 h, then returning quickly to baseline (12). However, the findings of the current review disagree with this notion in the context of an HFM. We found that, of the studies that met the pre-established inclusion criteria, ~70% (19 of 28 studies) found no significant change in TNF-α after an HFM. Similar to CRP, the remaining
studies that did find a significant change were divided in terms of detecting a significant increase (5 studies) or decrease (4 studies). TNF-α is primarily produced by macrophages, such as those that populate inflamed regions of the vascular endothelium (6, 76). TNF-α is known to be an important mediator in both acute and sustained inflammation (76). Specifically, TNF-α can induce increased secretion of itself, as well as other proinflammatory cytokines, making it an important contributor to the amplifying nature of the inflammatory response (76). However, although it appears that TNF-α may be particularly responsive in an endotoxin model of inflammation, it is not very responsive to HFM intake. Because 23 of 28 studies assessing postprandial TNF-α in the present review found either no change or a significant decrease after an HFM, it appears that TNF-α is either not sufficiently responsive to an HFM stimulus or is too variable in its assessment to be deemed a reliable marker of inflammation in the hours after HFM intake.

Although the majority of included studies did not find a significant change in CRP or TNF-α, it is interesting that there was disagreement with regard to the directionality of the change in studies that did detect significant differences. This could possibly be driven by the composition of the test meal characteristics. With regard to meal composition, previous evidence suggests that type of fat (77), macronutrient distribution (35), and overall nutrient density (78) of the meal can alter the postprandial inflammatory response. Nevertheless, there were no clear, common differences between studies that found an increase compared with a decrease in CRP or TNF-α in the current review. Overall, due to the heterogeneity of study designs (especially test meal composition), this review is not well equipped to accurately identify the meal characteristics that induce inflammation. On the contrary, the goal of this review was to summarize the overall post-HFM inflammatory response. Although there are potentially certain nuances and influential factors that likely affect the response, the data synthesized in the present systematic review strongly suggest that CRP and TNF-α do not typically change in the acute hours after HFM consumption.

The remaining markers of inflammation assessed in the present study, IL-1β and IL-8, were rarely measured in the acute postprandial period in healthy individuals (IL-1β, 3 studies; IL-8, 4 studies). Because few studies analyzed these markers, we cannot make firm conclusions with regard to their activity in the hours after a meal. However, our findings do not suggest that these markers robustly change after the consumption of an HFM, because 2 studies found no change in IL-1β post-HFM and 1 found a significant decrease, and 3 studies found no change in IL-8 post-HFM and 1 found a significant increase. Despite being less frequently assessed, IL-1β and IL-8 are both considered proinflammatory cytokines that play adverse pathophysiologic roles in CVD development, recruiting immune cells to the site of vascular damage as well as promoting increased production of other proinflammatory cytokines (79). IL-8 is produced from a variety of cells, including monocytes, macrophages, T lymphocytes, and endothelial cells (80), whereas IL-1β is produced primarily by activated macrophages. Similar to TNF-α, although IL-1β and IL-8 are produced locally at the site of damage, they do not appear to transiently and/or robustly change in the postprandial period after the consumption of an HFM.

Strengths and limitations. There are several strengths to the present systematic review. First, we used a robust systematic search of 10 relevant databases with a search strategy developed with the assistance of a librarian (CL). The relatively large number of citations found with the original search (494 citations), in addition to the number of duplicate citations found by multiple databases (164 duplicates eliminated), suggests that the search was comprehensive and that it is unlikely that many, if any, relevant articles were not captured with our systematic search. Next, our generally broad yet clearly defined inclusion criteria ensure that our findings are applicable to many people, namely healthy men and women between the ages of 18 and 60 years, independent of geographic region and body weight status. Finally, a strength of this study lies in its research and clinical utility. This systematic review represents the first attempt, to our knowledge, to clearly quantify the specific changes in commonly assessed markers of inflammation in response to an HFM. However, this review is not without limitations. As with any systematic review, it is possible that we may have missed ≥1 pertinent study. In addition, not all of the studies that met our inclusion criteria provided all of the information needed to help answer our research question. Although all of the authors whose articles had missing data were contacted in an effort to retrieve those data, and many authors complied and submitted their data to us (see Acknowledgments), not all responded, and consequently some studies are still missing important information such as peak and time to peak responses for an assessed cytokine. Next, the external validity of our findings are limited to healthy adults. Individuals with disease will typically present with a high systemic inflammatory tone; therefore, the postprandial inflammatory response may be more dramatic in these populations. In addition, it should be noted that most studies included in the present systematic review assessed postprandial inflammation for 4–8 h after HFM intake. Thus, our review is not equipped to describe any inflammatory marker changes that could potentially occur outside of that typically used window of time. Next, an additional analysis with regard to the relation between the type of fat or meal in determining the postprandial inflammatory response would have been informative. However, due to the heterogeneity of test meals and the manner in which they were reported, this point was not possible for the present systematic review to address in a qualitative analysis. Qualitatively, however, there do not appear to be any noticeable trends between studies that found an increase in a marker and those that found no change other than that most studies used meals reflective
of the Western-type diet, which is high in animal (saturated) fats, simple carbohydrates, processed foods, and kilocalories and low in fruit, vegetables, whole grains, and fiber. Finally, a frequent consideration with postprandial metabolic and inflammatory response research is the use of test meals that are not necessarily representative of meals that individuals might consume during normal daily living. Consequently, this systematic review contained many studies with test meals that were quite large, energy-dense, and high in fat (Table 1, Supplemental Tables 1–4). This point should be considered when interpreting and drawing conclusions from the present data.

Conclusions and future directions. This systematic review aimed to characterize the postprandial response of 5 commonly assessed markers of inflammation after the intake of an HFM. Our findings suggest that only 1 of those 5 markers, IL-6, consistently increases in the 4–8 h post-HFM. Specifically, IL-6 will, on average, start at a baseline of ~1.4 pg/mL and peak at ~2.9 pg/mL ~6 h later. In relative terms, IL-6 will increase by ~100% in response to an HFM. Of the potential independent variables considered, only the percentage of fat in the test meal showed a significant (negative) correlation with the percentage change in IL-6 post-HFM, although a linear regression model including age, BMI, percentage of fat in the test meal, and energy content of the test meal was found to significantly predict the percentage change in IL-6. With regard to CRP and TNF-α, these markers were found to be very commonly assessed in the postprandial period, although they rarely showed any change. IL-8 and IL-1β also infrequently changed after HFM consumption in healthy individuals, although these markers have only been assessed in a few studies. In light of these findings, we have the following several recommendations for future research: 1) we suggest that CRP and TNF-α no longer be assessed for postprandial changes in healthy individuals within the normal 6–8 h postprandial time course; 2) instead, there may be more merit in assessing other inflammatory markers, such as leukocyte-bound markers, in healthy individuals exposed to an HFM, because they may be more likely to show postprandial changes (12); 3) a similar review focusing on the postprandial inflammatory response of individuals with disease is warranted, because the results could very likely differ from the present review that focused on healthy individuals; and 4) further investigation into the specific role that IL-6 plays after HFM intake would be beneficial.

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