Psoriasis is a common inflammatory condition involving the skin, scalp, nails, and joints. It significantly increases the risk of cardiovascular events and death in those affected, above Framingham Risk Score prediction alone. There is a dose-response element; those with the most severe psoriasis (assessed by the psoriasis area severity index score) are at the greatest risk. A UK study estimated the excess risk as being equivalent to having a diagnosis of diabetes mellitus.2 Psoriasis often becomes apparent at a young age, exposing patients to higher risk for several decades. This translates into a lifetime excess of cardiovascular mortality of \( \approx 2.3 \) aortic valve stenosis and arterial stiffening, both conditions believed to have inflammatory bases.5,6

In this edition of *Atherosclerosis, Thrombosis, and Vascular Biology*, Naik et al7 measured vascular inflammation in a group of 60 subjects with mild to moderate psoriasis and compared their findings to control subjects. They hypothesized that the extent of vascular inflammation, quantified with fluorodeoxyglucose positron emission tomography (FDG PET) imaging, would be related to the severity of psoriasis, estimated by the psoriasis area severity index score. They also gathered evidence in support of their belief that the well-recognized links between psoriasis and vascular disease might be mediated by inflammation via neutrophils. The recruits were relatively young, although they had suffered psoriasis for a median of 20 years. Many were already receiving systemic psoriasis therapy at the time of PET imaging. Overall, the group was classified as low-risk according to Framingham Risk Score. Their findings were instructive. First, FDG uptake was greater in psoriasis patients than in controls, with target-to-background ratio values suggestive of at least moderate arterial inflammation.4 Psoriasis severity was significantly positively associated with vascular inflammation, even after adjusting for Framingham Risk Score and C-reactive protein levels. Supportive of their second hypothesis, psoriasis patients had significantly higher levels of neutrophil-associated cytokines than control subjects, and in particular, S100A8/A9 (an endogenous toll-like receptor 4 activator protein–binding complex) was related to both psoriasis severity and arterial inflammation.

FDG PET has been used to measure vascular inflammation in many inflammatory conditions, including rheumatoid disease (where it also demonstrated that systemic therapy lowered vascular inflammation),9 chronic obstructive pulmonary disease,10 and most widely atherosclerosis, where it highlighted the beneficial effects of statin therapy on the vessel wall11 and can predict clinical events.12 Because FDG accumulation and retention within the vessel wall reflects glucose usage, many cell types located there can influence the final signal. In the hypoxic atherosclerotic plaque microenvironment, macrophages predominate,13 particularly once activated.14 In psoriasis, the cell type responsible for vascular FDG uptake is unknown.

Does systemic psoriasis therapy influence surrogate markers of cardiovascular risk? In a small study that recruited patients with severe psoriasis and measured carotid and brachial arterial intima–media thickness, therapy with etanercept, infliximab, or adalimumab did result in significant regression of intima–media thickness measurements, but this was restricted to those without established atherosclerosis at baseline.15 Bissonnette et al16 used vascular FDG PET as a marker of inflammation, but failed to meet their primary end point in a larger, randomized study with the potent anti-inflammatory drug adalimumab. Interestingly, a retrospective study by Prodanovich et al showed that patients with psoriasis treated with methotrexate had decreased rates of vascular disease when compared with controls.17 It will be instructive to see whether the same holds true in the Cardiovascular Inflammation Reduction Trial that will randomly allocate 7000 patients with prior myocardial infarction and either type 2 diabetes mellitus or the metabolic syndrome to low-dose methotrexate or placebo over an average follow-up period of 3 to 5 years.18

**Summary**

This work extends the use of imaging to uncover potentially important links between 2, on the face of it, different conditions. It seems plausible that, as the authors suggest, smouldering skin lesions produce inflammatory cytokines that can trigger remote inflammation. This has recently been reported, albeit in reverse, after myocardial infarction, where global inflammation is upregulated after an acute coronary syndrome putting patients at high risk of recurrent events.19 Naik et al’s study was cross-sectional, and as acknowledged by the authors, their hypotheses need to be confirmed or refuted by ongoing longitudinal studies to prove cause and effect.

In terms of psoriasis management, their study elegantly illustrates the paradox of significant vascular inflammation.
yet low Framingham scores and provides an explanation for it via neutrophil-mediated inflammation. Whether psoriasis patients should undergo testing for subclinical atherosclerosis21 or receive aggressive statin therapy is not known, but the case is strengthened by this article. By providing mechanistic insights between psoriasis and atherosclerotic inflammation, this study suggests new therapeutic targets that could be exploited to lower the excessive cardiovascular disease burden that these patients experience.

Sources of Funding
J.M. Tarkin is supported by a Wellcome Trust research fellowship (104492/Z/14/Z) and the NIHR Cambridge Biomedical Research Centre. J.H.F. Rudd is part-supported by the HCEFCE, the NIHR Cambridge Biomedical Research Centre, the British Heart Foundation, and the Wellcome Trust.

Disclosures
None.

References
Psoriasis: More Than Just Skin Deep
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*Arterioscler Thromb Vasc Biol.* 2015;35:2487-2488
doi: 10.1161/ATVBAHA.115.306560

*Arteriosclerosis, Thrombosis, and Vascular Biology* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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