IgM-rheumatoid factor is associated with skin temperature in a patient with longstanding rheumatoid arthritis: a 6-year time series pilot study

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Abstract
The objective of this study was to determine the relationship between skin temperature and the level of IgM-rheumatoid factor (RF) in a patient with rheumatoid arthritis (RA). This n=1 pilot study was self-performed (63-year-old man, RA-patient, IgM-RF-positive). Simple measures were applied for skin cooling, like light clothing and being outdoors. Skin temperature was measured every 5 min (24/7) on 1,635 days at the right wrist using a miniature temperature logger. Blood values of IgM-RF, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and anti-citrullinated protein antibodies (ACPA) were collected routinely.

In the first measuring period (A in figure 1A), the Spearman correlation coefficient between IgM-RF and the mean skin temperature of the 13 preceding weeks was unexpectedly high (r=0.80, n=16, P<0.001). Using longer or shorter periods than 13 weeks resulted in a decline of r. The experiment was repeated (B in figure 1A) and again a high correlation was found (r=0.83, n=42, P<0.001). In period B, the IgM-RF decreased to below the reference value (<16 IU/ml).

This pilot study argues that IgM-RF is associated with skin temperature in a single RA-patient.

Introduction
Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) are antibodies that play a key role in rheumatoid arthritis (RA) [1]. Recent studies show that IgM-RF enhances ACPA-pathogenicity leading to an increased level of disease activity and bone erosion [2] [3]. Hence, reduction of the IgM-RF level is crucial to ACPA-positive RA-patients and their seropositive first-degree relatives as well [4]. Being an RA-patient myself (63-year-old man [in 2010], PhD in physiology, RA since 1979, IgM-RF- and ACPA-positive, 8 joint prostheses) I noticed that my IgM-RF showed the tendency to increase in warmer periods and to decrease in the cold. Until now most studies of temperature effects on RA-variables made use of the meteorological temperature, exemplified by a recent study on the possible effect of temperature on RA-symptoms [5]. This will result in a disturbed view of the relationship since, in hot regions, many patients live in a cool air-conditioned environment, while in cold climates, patients often feel comfortable in heated housing. Therefore, in the present self-performed pilot study, the temperature of the skin is measured. In this way, all possible influences on skin temperature, like degree of clothing, all weather circumstances, indoors or outdoors, local skin blood flow, exercise, and sleep are taken into account. The association of IgM-RF with skin temperature is investigated.

Objective
Being a patient with rheumatoid arthritis (RA), my objective was to conduct a pilot study to determine the relationship between skin temperature and the level of IgM-rheumatoid factor (RF).
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Figure Legend
Figure 1. Associations of skin temperature with outdoor exposure to cold, and with IgM-RF.
(A) Relations between skin temperature and clinical parameters.
Mean daily skin temperature (right wrist) of the preceding 13 weeks (solid line), and 4 weekly blood levels of IgM-RF (circles) (asterisk: <16 IU/ml), ESR (squares), and CRP (triangles). The strong increase of skin temperature in 2013 was caused by ill health (pneumonia), which interrupted the exposure to cold. The same is applicable to the increased skin temperature after joint surgery on April 22, 2010 (marked by the CRP/ESR peak) with subsequent rehabilitation. Other ESR/CRP peaks were due to transient allergic reactions, likely to food components.
(B) Example of 24-h course of the skin temperature.
This curve (July 2, 2014) illustrates the strong variation in the skin temperature. The labelled black horizontal bars indicate periods outdoors. Especially cycling outdoors lowers the temperature while the highest temperatures are measured during night-time. The gap in the curve marks discarding of readings obtained when the logger was removed briefly (shower).

Results & Discussion
Skin temperature data were weekly obtained by reading out the miniature temperature logger. Daily 24 h mean skin temperatures were calculated after discarding the readings obtained when the temperature logger was removed briefly (showers and data readout). The correlation between IgM-RF and the mean skin temperature of the 13 weeks preceding each blood sampling (Fig. 1A, Period A) was unexpectedly high (r=0.80, n=16, P<0.001). Using longer or shorter periods than 13 weeks resulted in a decline of r. This result suggests that IgM-RF is associated with the mean skin temperature of the foregoing 13 weeks. The finding prompted continuation of the cold lifestyle, as mentioned above, now as a potential therapy.

On June 10, 2012, logging of skin temperature was resumed. In figure 1B, an example of the 24 h course of the skin temperature is given. Periods outdoors (with or without increased exercise) are accompanied by direct and clear decreases in skin temperature. Gradually, more cooling was tolerable due to habituation (Fig. 1A, Period B). Again a high correlation was found between IgM-RF and the mean skin temperature of the preceding 13 weeks (r=0.83, n=42, P<0.001). ARIMA-modeling of periods A and B together showed that 1℃ decrease in mean skin temperature correlated with a significant reduction of IgM-RF with 25.4 IU/ml. Eventually, IgM-RF was reduced from 75 IU/ml (July 2010) to below reference level (<16 IU/ml) in September 2015. Medication was kept stable (methotrexate 15 mg/week, folic acid 5 mg/week, indomethacin 75 mg/day) since 2003 and during the present study, except for adalimumab (tumour necrosis factor [TNF] inhibitor, see bottom Fig. 1A). End of November 2015, logging of skin temperature was stopped but the cold lifestyle was continued.

Of course, skin cooling is one of many factors that can play a role in the reduction of IgM-RF. Increased exercise or otherwise changed lifestyle might contribute as well. However, in the present study, the association with skin temperature is apparent.

Conclusions
This pilot study suggests an association between IgM-RF and skin temperature in a single RA-patient. In this cold lifestyle study, the IgM-RF was eventually lowered to below the reference value.

If the effects found in this pilot study turn out to be reproducible in other RA-patients, a cold lifestyle could become a safe and low-cost addition to RA-treatment.

Limitations
Although a large time series of measurements were done in the present study, all data were collected from only a single subject (the author). This might raise doubts about introduction of study bias due to auto-sampling. However, blood was sampled and analysed in an accredited diagnostic laboratory, and logging of skin temperature was...
fully automated. A display was lacking, so the author was not aware of the actual skin temperature. The logger was read out once a week which was a necessary check on the proper operation of the temperature logging system. Finally, randomisation is not possible in this study, but surely must be applied in a follow-up study on a group of IgM-RF-positive RA-patients.

Additional Information

Methods and Supplementary Material
Please see https://sciencematters.io/articles/201804000007.

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Ethics Statement
Not Applicable.

Citations