CLEARANCE OF I\textsuperscript{131} INJECTED INTRALESIONALLY IN PATIENTS WITH PSORIASIS\

EDWARD H. FERGUSON, M.D. AND WILLIAM L. EPSTEIN, M.D.

Vascular changes undoubtedly play a significant role in the pathogenesis of psoriasis. The present study concerns the local hemodynamics of psoriatic plaques measured by skin clearance of radioactive substances. This method gives a rough measure of local vascular dynamics (1–7), and, despite any shortcomings, probably supplies a more realistic picture than does use of colorimetry or plethysmography (3).

MATERIALS AND METHODS

Fourteen patients with psoriasis, ranging in age from 18 to 64 years, were examined at rest in a room temperature environment that did not vary over 1°F. Each subject served as his own control. Sixty observations of clearance times were made from psoriatic plaques and 54 from control areas. In 26 additional non-psoriatic subjects, clearance times were determined in 65 instances following injection of pharmacologic agents such as histamine, Histalog (8) and 48:80; 52 control readings were made in this group.

Iodine\textsuperscript{131} as sodium iodide in solution (20 uc/ml.) was injected intradermally into the center of small psoriatic plaques and into uninvolved areas of skin. Each injection contained 0.05 ml. (1 uc). Radioactivity was detected by means of a sodium iodide crystal equipped with a flat field collimator attached to a Nuclear-Chicago Ultrascaler, Model 192 A. The collimator was placed directly over the injection wheal in light contact with the skin. Counts per minute were calculated every \(1/4\) minutes starting 3 minutes after injection.

Most observations were made on the thigh where results generally were reproducible. Measurements around joints and in acral areas yielded results that were variable and generally unsatisfactory. We avoided lesions on the trunk due to inability to immobilize test sites. Control test sites were located near the psoriatic plaque or in an identical site on the opposite extremity. At least 4 to 6 observations were made on each subject.

The logs of the counts per second were determined from these data and recorded on semi-log graph paper; the result was a straight line. The time in minutes after injection for the counts to fall to one-half the initial reading was designated \(T_{1/2}\). It reflects the rate of clearance (3).

RESULTS

I\textsuperscript{131} invariably disappeared from acute or chronic psoriatic plaques more rapidly than from uninvolved skin. An example of the pattern of clearance is shown in Fig. 1. In this instance the \(T_{1/2}\) for the psoriatic lesion (2.9 min.) was about one-third that for uninvolved skin (9.2 min.). The average clearance rates for all active psoriatic plaques and their controls are compared in Table I. The average difference between the \(T_{1/2}\) times of controls and plaques (6.9 min.) indicates the marked change in hemodynamics of the psoriatic lesion. In a situation where the \(T_{1/2}\) from uninvolved skin averages 10.7 min., this becomes a highly significant measurement. On the other hand, clearance rates from uninvolved skin of psoriatic patients followed the same pattern as they did in normal subjects. The \(T_{1/2}\) from wheals produced by injections of histamine, histalog or 48:80 showed a slight, probably insignificant, decrease over control readings (Table II). The increased clearance from ultraviolet light-induced erythema and from lesions of erythema multiforme was not of the same order as that seen in psoriasis. No patients with generalized seborrheic dermatitis were tested.

The question of possible lateral spread was tested by means of autoradiographs taken over injection sites. I\textsuperscript{131} (100 uc/0.05 cc.), was injected as before into normal skin and into psoriatic plaques. Then unexposed dental film was applied to the skin surface, protected by a thin lead screen to give sharper definition. The film was changed every two minutes for twelve minutes. No lateral spread was detected. In fact, the spot of radioactivity disappeared from the psoriatic patch after the second film, but remained in all films over uninvolved control skin.

To test whether or not our findings were unique for iodine, Na\textsuperscript{22} as sodium chloride (8 uc/ml.) was injected into psoriatic plaques and control sites. The pattern of clearance from both uninvolved and psoriatic lesions followed that seen with

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Fig. 1. A comparison of the rate of clearance of I\(^{131}\) from a psoriatic plaque and control site in the same patient.

**TABLE I**  
Active plaques

<table>
<thead>
<tr>
<th>Site</th>
<th>Number of Comparative Observations</th>
<th>(T_{1/2}) Times in Minutes</th>
<th>(T_{1/2}) Times in Minutes Average Differences Plaques &amp; Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thigh</td>
<td>16</td>
<td>12.7</td>
<td>4.3</td>
</tr>
<tr>
<td>Upper arm</td>
<td>5</td>
<td>7.4</td>
<td>3.5</td>
</tr>
<tr>
<td>Elbow</td>
<td>2</td>
<td>8.2</td>
<td>3.2</td>
</tr>
<tr>
<td>Knee</td>
<td>1</td>
<td>11.5</td>
<td>5.3</td>
</tr>
</tbody>
</table>

Average of differences = 6.9 minutes.

**TABLE II**  
Average differences of \(T_{1/2}\) times between test areas and uninvolved control sites

<table>
<thead>
<tr>
<th>Test Sites</th>
<th>Number of Comparative Observations</th>
<th>Difference in Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis (active plaques)</td>
<td>24</td>
<td>6.9</td>
</tr>
<tr>
<td>Histamine Histalog and 48:80 wheals</td>
<td>56</td>
<td>0.7</td>
</tr>
<tr>
<td>3/4 hour to 2/3 hours after ultraviolet light</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Erythema multiforme drug eruptions</td>
<td>3</td>
<td>3.4</td>
</tr>
</tbody>
</table>

 appearantly the observations have general significance in regard to local fluid dynamics.

Involuting psoriatic lesions showed a consistent prolongation in clearance time. The \(T_{1/2}\) times approached those of uninvolved skin (Table III). The return toward normal was not conditioned by the type of therapy; it occurred whenever the lesions began to heal. The rate of change toward normal was studied by determining the clearance times in psoriasis plaques at intervals after the intrallesional injection of triamcinolone (Table IV). By two days, when the lesion was just beginning to heal, the clearance time had markedly decreased. During the next seven days—despite almost complete clinical clearing of the lesion—no further change was observed in the rate of \(T_{1/2}\) clearance. This finding suggests that vascular
dynamics can be expected to change more rapidly than epidermal metabolism. The precise time of return to a completely normal blood flow was not determined, but by a year the mildly atrophic injection site responded normally.

Four patients were examined periodically during flares and remissions. The fluctuation of skin clearance correlates well with fluctuations in activity of the disease. An example is presented in Fig. 2. In one instance an increased clearance rate was noted in a clinically healing lesion. Within a week the lesion had flared up, suggesting that determination of the $T_{1/2}$ time may have prognostic value.

**DISCUSSION**

Despite much excellent work, psoriasis remains a disease of unknown etiology. Even the primary site of involvement has not been established (9, 10). Although some work tends to implicate the epidermis (11), a number of investigators feel the dermis and dermal vasculature are the nascent sites of the disease (12-14). Unquestionably the blood vessels play a significant role in the genesis of psoriasis as a pathologic entity (10, 15-23). Capillaries are dilated and tortuous (24-27); the view with a capillary microscope is characteristic (10, 15, 26, 28, 29). The changes appear before recognizable epidermal changes (10) and persist after healing (15). Even with ordinary histological methods, a persistence of vascular changes after clinical clearing has been demonstrated (30, 31). The function of these vessels, however, has received little attention. Aside from a delayed onset of reactive hyperemia in uninvolved skin of psoriatics (32, 33) and some questionable changes in plethysmographic patterns of digits (34), no functional abnormalities have been described. Blood flow through the digits is reported as normal (35).

Herrmann and Kanof demonstrated a fluorescent halo surrounding psoriatic lesions after intravenous injection of fluorescein (36). The lesions themselves remained dark, and although these workers recognized that a thick scale could mask fluorescence, they speculated that a sluggish circulation might also explain the phenomenon.

Our results do not substantiate this view. We have observed a remarkably rapid disappearance of $^{131}$I from psoriatic lesions. Certainly the lymphatics play a role in clearing $^{131}$I. However, considering the anatomical findings of vascular dilatation and the rapidity of clearance, which is not characteristic of lymph flow, we view the blood vessels as the major determinant of $^{131}$I clearance in this instance. Blood flow through psoriatic plaques seems exceedingly rapid, and this may help explain the high state of metabolic activity of the lesion (17, 37-39). In healing, changes in vascular physiology probably precede epidermal changes.

**SUMMARY**

The blood flow in psoriatic plaques is increased as indicated by an increased clearance rate of locally injected radioactive salt solutions. This functional abnormality tends to vanish with involution of the lesion.

**ACKNOWLEDGMENTS**

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The authors wish to thank Kenneth G. Scott, Ph.D., Director of Radioactivity Center, University of California, San Francisco Medical Center, for his advice and criticism.

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DISCUSSION

Dr. Eugene J. Van Scott (Bethesda, Mary-
land): Your data, of course, does suggest that
there is an increased blood flow through the lesion
of psoriasis. Yet, the epidermis of psoriasis, com-
pared to normal, is several fold thicker than nor-
mal and the thickness of the epidermis may
approach a half millimeter. How does one gauge
the depth to which this material is injected and
how does depth of injection influence the disap-
pearance rate?

Dr. Peter Flesch (Philadelphia, Pennsyl-
vania): Wouldn't the thickness of the epidermis
influence the count?

Dr. Stephen Rothman (Chicago, Illinois): Histamine is not an appropriate substance for
testing the effect of vasodilation because it also
causes exudation which in its turn compresses the
dilated minute blood vessels. Pure vasodilators
such as acetylcholine or priscoline could be used
to decide whether pure vasodilation causes such
great increase in clearance as was observed by
the investigators in psoriasis.

Dr. Edward H. Ferguson (in closing): I wish
to thank the discussors.

In answer to Dr. Van Scott and Dr. Flesch,
the depth of injection (and particularly in the
thickened psoriasis plaque), does influence the
count.

However, what we are doing is comparing the
rate of fall off, not the exact counts. This is one

reason the individual must serve as his own control. Although it wasn’t true in some instances, usually the count was slightly lower in the psoriasis plaques.

Now as far as iodine within a skin lesion is concerned, we are injecting $^{131}$I and watching its disappearance, which is a matter of a very short time. We are talking about it becoming half what it was in anything from two and a half minutes to twelve or fifteen minutes, depending upon the lesion we are dealing with. Total iodine content and iodine metabolism will have no bearing on the results. We feel that the clearance is by way of blood vessels and that this method is a good rough measure of the effectiveness of the local circulation. (References 1–7).

As far as Dr. Rothman’s question about using a good vasodilator as a control, I think this is a very good point.

We did, of course, use epinephrine and like everyone else who has used this sort of technic, we got a decrease and, in fact, practically a complete cessation of clearance (References 1 & 2). Priscoline has been shown to increase the clearance rate. (Freund, J., Wisham, L. H., and Yalow, R. S.: The Effect of Priscoline on the Clearance of Radiosodium from Muscle and Skin of Man in Normal and Diseased Limbs. Circulation. 8: 89, 1953).

We did demonstrate with hyaluronidase that diffusion could give some increase in disappearance time but it wasn’t of the same order as that seen here. With hyaluronidase, this has been demonstrated previously by Forbes et al. (Forbes, G., Deisher, R. W., Perley, A. M., and Hartmann, A. F.: Effects of Hyaluronidase on the Subcutaneous Absorption of Electrolytes in Human Science 111: 177, 1950).