

DIFFERENTIAL TISSUE AND ORGAN ANOXIA IN DISEASE: THE MEASUREMENT OF PERI- ARTICULAR OXYGEN SATURATION LEVELS IN PATIENTS WITH ARTHRITIS*

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Introduction

A number of investigations testify to the association of vascular factors with joint disturbances. The Scientific Advisory Committee of the Empire Rheumatism Council concluded, as a result of a carefully controlled investigation (1950), that peripheral vascular abnormalities are not only associated with rheumatoid arthritis but frequently ante-date its onset; Davis (1941) analysed 88 cases in 27 families in which spontaneous ecchymoses had occurred, and concluded that an intimate relationship exists between arthritis and purpuric manifestations; Fletcher (1947) states that patients with rheumatoid arthritis usually have cold, clammy hands, the skin of which assumes the temperature of its surroundings sooner than the skin of normal persons, while the reaction to heat and cold is poor and slow. Increased periarticular vascularity, perivascular lymphocytic infiltration of the synovial membrane, and periarticular rheumatic arteritis resembling periarteritis nodosa, are described as typical of the pathology of rheumatoid arthritis. Factors connected with the functions of the capillaries have been investigated in cases of arthritis and abnormalities described: thus Race (1937) found a low blood ascorbic acid level in patients with all types of rheumatism, and Fletcher (1947), commenting on Race's work, remarks:

although it is fairly clear that lack of vitamin C is not the cause of rheumatoid arthritis, it may well be one of the factors concerned in its production.

Vitamin K has been similarly implicated, Rawls and others (1935) having described a low prothrombrin level in half their series of patients with rheumatoid arthritis. As with function, so with structure: capillary spasm, slowed blood flow, and distortions of the normal morphological capillary patterns, have all been described (Fox and Van Breemen, 1934). Finally, the local treatment of rheumatic disorders by means of oil of wintergreen and other rubefacients, injection of thio-histamine, massage, ultra-violet light, and various types of heat application from infra-red to hot wax baths, is treatment acting primarily on the vascular components of the disease process and achieves a success which is often in direct relationship with its efficacy in this respect.

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The present study attempts the investigation of a further variable of the vascular complex comprising the local components of the arthritic process, i.e. that concerned with the periarticular oxygen metabolism.

Experimental Methods and Clinical Material

Two oximetric techniques were used concurrently. The Millikan photo-electric oximeter (Millikan, 1942) was used to determine the arterial blood oxygen saturation levels of the general circulation (recording from the minute vessels of the pinna of the ear) after preliminary flooding of the circulation with 100 per cent. oxygen by inhalation through a mask to standardize the instrument. With such equipment Millikan obtained agreement to within ± 5 per cent. in the upper range against *in vitro* Van Slyke manometric determinations made on blood withdrawn from human subjects by arterial puncture.

For the periarticular determinations, a modification (Lovett Doust, 1951) of the "Reduction Time" method described by Ray (1946) was used. In contrast with the continuous oximetric analysis carried out by the Millikan instrument, the reduction time or spectroscopic oximetry technique is discontinuous and dependent upon the fact that the absorption bands of oxyhaemoglobin, when observed from heated, illuminated, histaminized skin through a pocket spectroscope, disappear after occlusion of the peripheral circulation at a rate proportional to the degree of saturation of the haemoglobin with oxygen. It was found to be possible to train the spectroscope on any reasonably thin area of skin of the hands or wrists and to get highly reliable results. Using the skin of the dorsum of the hand in a large number of healthy subjects, Ray (1946) found a correlation coefficient of $+0.87$ between the reduction time and the alveolar oxygen tension.

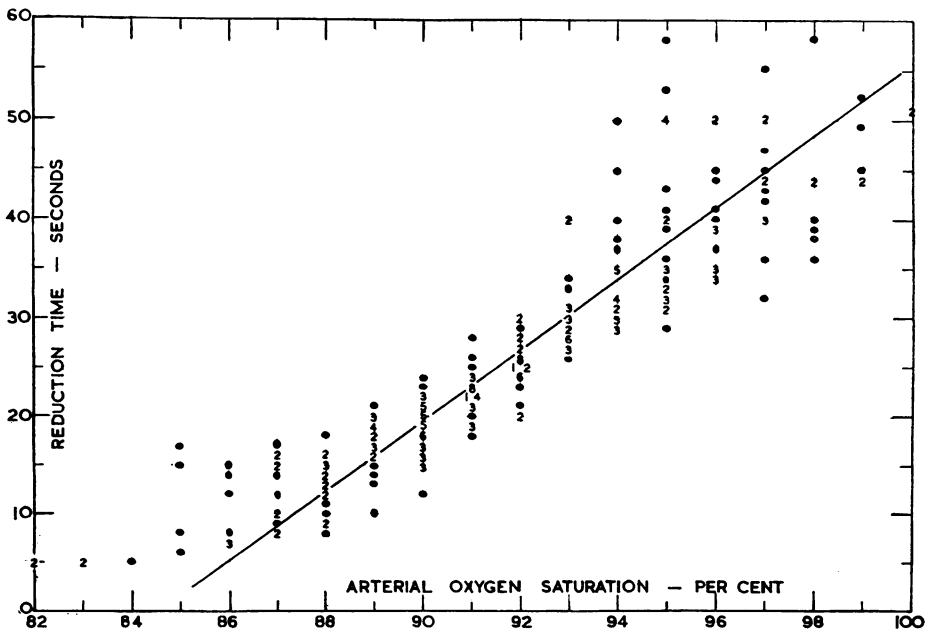


FIG. 1.—Calibration graph of 285 simultaneous oximetric determinations made on healthy, non-arthritic subjects.

Ordinates are results obtained by spectroscopic reduction-time method on skin vessels of finger, expressed in seconds. Abscissae are results obtained by the photo-electric oximeter on vessels of pinna of ear in percentage arterial oxygen saturation. Line of regression obtained from a regression equation yielded a correlation coefficient of $+0.92$.

Cross correlation of the two methods of oximetry, in a series of 285 simultaneous observations by the present writer (Fig. 1), shows a satisfactory degree of agreement between them ($r = +0.92$).

In the present investigation, periarticular oximetry was carried out by focussing the spectroscope on the skin around the various joints of the fingers and hands.

Control Group.—The joints chosen were the proximal interphalangeal joint of the left ring finger (L.4 p.i.p.) and the distal interphalangeal joint of the left index finger (L.2 d.i.p.). This was an arbitrary and convenient choice of location. The results in this group for all periarticular regions of the fingers were similar for any one individual and at any one time wherever the measurements were taken, always providing no local skin lesions were present and no pathology was involving the joint under investigation.

The controls were a group of 35 apparently normal healthy subjects of both sexes whose ages ranged from 18 to 46 years. They were investigated in exactly the same way as the patients with arthritis.

Patients.—This was an unselected group, the only criterion for inclusion being an unequivocal diagnosis of some form of arthritis affecting the joints of the fingers. Most patients suffered from the rheumatoid type of atrophic arthritis but few were uncomplicated by other conditions (Table I). There were eight females and two males in the series and their ages ranged from 15 to 62 years. They all had objective clinical evidence of their disability, varying from slight degrees of swelling, pain, and limitation of movement in one or more joints up to gross deformities affecting practically all joints of both hands

TABLE I
BASIC DATA ON TEN CASES OF ARTHRITIS AND 35 HEALTHY CONTROLS

Case No.	Sex	Age (years)	Arterial Blood Oxygen Saturation per cent.—Range			Local Clinical Activity (4-point scale)	Principal Diagnosis	Ancillary Diagnoses
			General blood stream (ear)	Joints				
				Unaffected	Affected			
1	M	19	93-95	91-94	86-92	+	*R.A.	Postural scoliosis Emotional immaturity
2	F	18	92-96	92-96	88-90	++	R.A.	Muscle tension syndrome
3	F	39	96-97	96-97	85-86	++++	R.A.	Osteo-arthritis Tinnitus Dyspepsia
4	F	36	95-96	94-95	90-91	++	R.A.	—
5	M	28	96-97	96-97	92-93	+	R.A.	Cervical osteo-arthritis Migraine
6	F	15	92-94	92-94	85-87	++++	Arthritis mutilans	Old Still's disease Cervical dislocation
7	F	62	91-94	91-94	89-92	++	R.A.	Osteo-arthritis Essential hypertension
8	F	29	97-98	97-98	92-93	+++	R.A.	Psoriasis
9	F	19	96-97	96-97	88-90	+++	R.A.	Pruritus Skeletal muscle tension syndrome
10	F	44	95-97	95-97	91-93	++	R.A.	Obstipation Corneal opacities Depression
35 Controls	15 F 20 M	18-46	93-98	93-98	—	—	—	—

* R.A.=Rheumatoid type of atrophic arthritis.

and many others elsewhere in the body. The youngest member of the group suffered from the sequelae of Still's disease contracted 3 years previously and *arthritis mutilans* was present to a very considerable degree: the patient could not walk and could stand, with support, only for periods up to 4 minutes at a time.

The spectroscopic and photo-electric techniques of oximetric examination were employed simultaneously, all measurements being checked until concordance was obtained, in the case of spectroscopic method, to within a difference of one second between the results in any one individual.

Results

These are shown in detail in Tables I to III and in Fig. 2.

Spectroscopic Oximetric Assay in Superficial Inflammation.—One member of the control group accidentally contracted a small acid burn on the finger-nail fold of the right middle finger during his work as a laboratory assistant. A small indolent abscess resulted, and an area a few millimetres in diameter was slightly warm to the touch, and red in colour with a tinge of blueness towards the periphery.

TABLE II
COMPARISON OF LOCAL CLINICAL STATE AND DEGREE OF
PERIARTICULAR ANOXIC INVOLVEMENT

Complete survey of finger joints of both hands in Case 6.
One finger (L. middle) was apparently completely spared: all the rest were severely affected.

Joint Examined	Right Hand			Left Hand		
	Reduction Time (secs.)	Equiv. O ₂ Saturation (per cent.)	Clinical Status	Reduction Time (secs.)	Equiv. O ₂ Saturation (per cent.)	Clinical Status
1 m.p.	23	91.5	SW.D.	14	88.5	D.P. & T.
1 i.p.	23	91.5	SW.D.	17	89.4	D.P. & T.
2 m.p.	21	91.0	SW.D.	20	90.5	SW.D.
2 p.i.p.	23	91.5	SW.D.	20	90.5	SW.D.
2 d.i.p.	19	90.0	SW.D.P. & T.	23	91.5	D.
3 m.p.	29	93.5	Normal	20	90.5	D.
3 p.i.p.	29	93.5	Normal	24	91.8	D.
3 d.i.p.	27	92.8	Normal	23	91.5	D.
4 m.p.	23	91.5	SW.D.	14	88.5	D.P. & T.
4 p.i.p.	23	91.5	SW.D.	18	89.7	D.P. & T.
4 d.i.p.	21	91.0	SW.D.	21	91.0	D.P. & T.
5 m.p.	15	88.8	SW.D.P. & T.	14	88.5	D.P. & T.
5 p.i.p.	15	88.8	D.P. & T.	11	87.5	D.P. & T.
5 d.i.p.	15	88.8	D.P. & T.	10	87.2	D.P. & T.

Topographic shorthand follows that of Fletcher (1947).

TABLE III

RESULTS OF LOCAL TISSUE OXIMETRY ON A SMALL ACID BURN OF FINGER-NAIL FOLD IN NORMAL SUBJECT

Effect of healing and correlation of oximetric analysis and clinical appearances.

Date	Oxygen Saturation per cent. General Circulation (photo-electric determination)	Local Tissue Oximetry of Lesion (spectroscopic method)		Remarks
		Equivalent O ₂ per cent.	Reduction Time (sec.)	
6.6.50	94-96	89.5	17	Indolent area of superficial inflammation. Calor et rubor
19.6.50	94-96	91.4	23	Healing satisfactorily
22.6.50	94-96	90.0	19	Reinfected by scratching
29.6.50	94-96	93.0	28	Healing
19.7.50	94-96	96.0	40	Healed

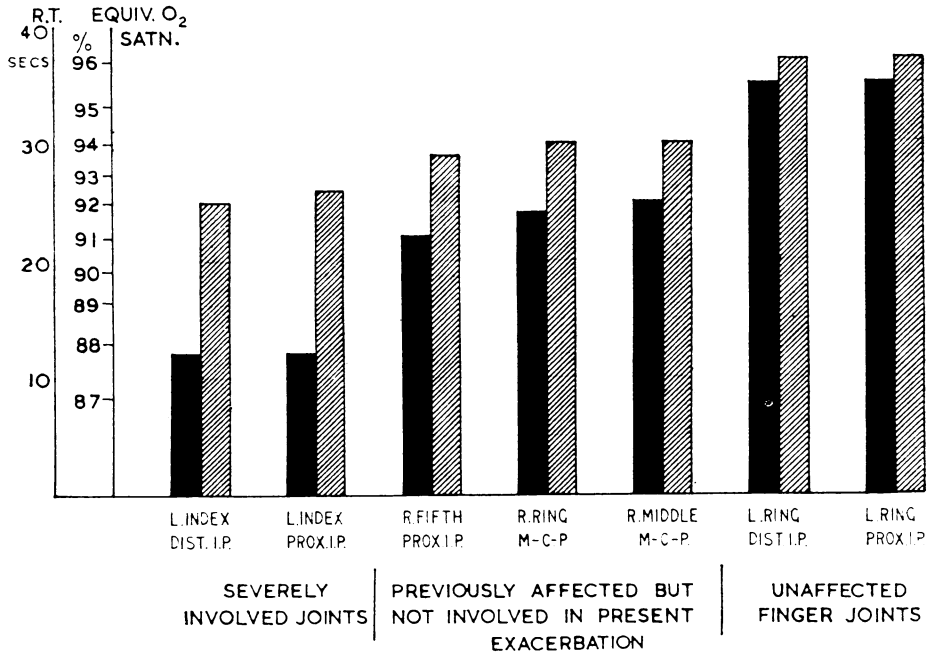


FIG. 2.—Female, aged 39 (Case 3). Results of a periarticular, spectroscopic, oximetric assay on three groups of joints (blackened histogram) compared with results of a repeated assay after inhalation by patient of 100 per cent. oxygen through a mask (hatched areas). Note periarticular anoxia of severely affected joints and concordance of clinical state with oximetric results.

Clinically it represented a very small disability and the subject had no thought of seeking treatment for it, discussing it as something which would heal unaided. Oximetrically, despite the turgor and apparent adequacy of blood supply, the lesion proved to be anoxic, although the blood of the skin vessels immediately beyond it showed a normal concordance with the arterial oxygen saturation levels of the general blood stream. Table III details these data and shows the changes taking place in longitudinal section as the lesion healed over a period of weeks.

Periarticular Oximetric Survey of Arthritic Finger Joints.—Complete surveys were made of all affected and unaffected finger joints in the ten cases of arthritis investigated. Such an individual assay occupied about 45 minutes for any one subject and required very little co-operation from the patient. The data obtained from the group are contained in Table I, which includes the mean results given by the control group for comparison. The individual results of an oximetric survey in a very severely disabled girl, in whom only one finger had been spared from a widespread and still active rheumatoid arthritis, are listed in Table II. A general correspondence between the level of local periarticular anoxia and the clinical intensity of the arthritic process was noted. Fig. 2 gives the partial results in histogram form of a similar survey in another case of rheumatoid arthritis.

Influence of Oxygen Inhalation.—Fig. 2 also shows the effects of inhaling 100 per cent. oxygen, through a B.L.B. type mask, on the periarticular oxygen saturation levels of anoxic arthritic joints. It will be observed that even grossly affected joints are capable of considerable oxaemic response, even up to levels within the critical range for normality.

Discussion

Objective methods of assessing the extent, degree, and capacity for change, of joint involvement in patients with arthritis have been lacking in the past, but recently a number of techniques have been introduced to this end. The four clinical tests of Quin and others (1950) have been criticized by Harris (1950) as unreliable, misleading, and not even objective, and the system devised by Steinbrocker and others (1949) can only handle gross changes taking place over a period of months. On the other hand, skin thermometry (Hartfall and Harris, 1949), and the technique of measuring blood flow described by Kellgren and Janus (1950), which depend upon all-important peripheral vascular factors, are not only quantitative but also completely objective. It would seem probable that the last two methods are influenced by the same variables as the method of oximetric assay reported here and the somewhat similar methodology suggested by Jarløv and Jarløv (1950).

It is also interesting to recall that the exhibition of oxygen has long been considered to be indicated in a number of different rheumatic disorders. Oxygen inhalation, breathing exercises, and the cautious transfusion of whole blood, are sometimes advised in the management and treatment of rheumatoid arthritis, while

for cases of sciatica and fibrositis, even the local subcutaneous *injection* of oxygen is stated to have proved successful in intractable cases (Copeman, 1947).

The spectroscopic oximetry technique described here would appear to provide a rapid and convenient method of objective assessment of the degree of involvement of arthritic joints. The results of such an oximetric assay could be used also to evaluate the prognostic implications involved in the differential reversal of the local anoxia by oxygen inhalation.

Summary

(1) Two methods of oximetry were employed concurrently to estimate the arterial blood oxygen saturation levels of the general circulation (photo-electric technique) and of the periarticular skin vessels (spectroscopic technique) around arthritic joints. Subjects included 35 healthy controls and ten patients with the rheumatoid form of atrophic arthritis.

(2) It was found that in patients with arthritis, though not in healthy controls, a dissociation between the oxygen saturation levels recorded by the two oximetric methods had occurred, the periarticular vessels showing a degree of anoxia which bore a relationship to the apparent degree of local clinical arthritic involvement. No generalized anoxaemia was found on routine examination in either patients or controls.

(3) It was found possible oximetrically and quantitatively to assay both superficial peripheral cutaneous lesions and the periarticular tissues of suspected arthritic joints for the presence of local anoxia. The advantages of such an objective method of assay in rheumatoid arthritis are discussed.

(4) It is shown that the anoxia around affected joints is temporarily reversible after the administration of oxygen by inhalation.

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**Anoxie Différentielle des Tissus et des Organes au Cours de la Maladie:
Mesure Périarticulaire des Points de Saturation par l'Oxygène chez les Malades
Atteints d'Arthrite**

RÉSUMÉ

(1) On s'est servi concurremment de deux méthodes oxymétriques pour déterminer les points de saturation par l'oxygène du sang artériel de la circulation générale (procédé photo-électrique) et du sang des vaisseaux de la peau (procédé spectroscopique) autour des articulations arthritiques. Trente-cinq témoins sains et dix malades atteints d'arthrite atrophique à forme rhumatismale furent soumis à cette étude.

(2) On a trouvé chez les arthritiques—mais pas chez les témoins—qu'il y avait une dissociation entre les points de saturation par l'oxygène déterminés par les deux méthodes oxymétriques; le degré d'anoxie constaté dans les vaisseaux périarticulaires était en rapport avec le degré apparent de l'atteinte clinique arthritique locale. L'examen régulier des malades et des témoins ne révéla pas d'anoxémie généralisée.

(3) On a trouvé qu'il était possible, oximétriquement et quantitativement, d'étalonner les lésions cutanées périphériques superficielles et les tissus périarticulaires des articulations suspectes par la présence d'anoxie locale. On discute les avantages de telles méthodes objectives d'étalonnage dans l'arthrite rhumatismale.

(4) On démontre que l'anoxie autour des articulations atteintes peut être supprimée temporairement en faisant inhaler de l'oxygène aux malades.

**Anoxia Diferencial de los Tejidos y de los Órganos en la Enfermedad:
Medición de los Niveles de Saturación Periarticular por Oxígeno en Artríticos**

SUMARIO

(1) Dos métodos de oximetría fueron empleados concurrememente para estudiar los niveles de saturación de oxígeno de la sangre arterial de la circulación general (técnica fotoeléctrica) y de los vasos periarticulares de la piel (técnica espectroscópica) alrededor de articulaciones artríticas. Los sujetos incluían 35 testigos saludables y diez enfermos con la forma reumática de atrofia artrítica.

(2) Se encontró que en los artríticos—mas no en los testigos—ocurría una divergencia en los resultados obtenidos por los dos métodos de oximetría, siendo de notar que los vasos periarticulares mostraban cierto grado de anoxia que estaba en relación con el aparente grado de desarrollo artrítico local clínico. En ninguno de los enfermos o testigos pudo encontrarse anoxemia generalizada durante el examen regular.

(3) Se encontró posible, oximétrica y cuantitativamente, el aquilatar las lesiones cutáneas periféricas superficiales y los tejidos periarticulares de articulaciones sospechosas de artritis por la presencia de anoxia local. Se discuten las ventajas que presenta un método tan objetivo para aquilatar la artritis reumatoide.

(4) Se demuestra que la anoxia alrededor de las articulaciones se puede suprimir temporalmente haciendo inhaler oxígeno a los enfermos.