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Effect of Inhaled Carbon Dioxide in Rheumatoid (Atrophic) Arthritis.

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A part of the limitation to movement in rheumatoid (atrophic) arthritis is due to muscle spasm and pain, not to limiting changes in structure. It can be lessened through administration of carbon dioxide and returned through acceleration of carbon dioxide loss (over-breathing) to a degree suggesting relationship to the phenomenon of hyperventilation tetany.

The 10 subjects of the experiment summarized in Table I were given inhalations of 10 to 15% carbon dioxide in oxygen for 2 to 5 minutes, from a Tissot spirometer, following determination of the degree of limitation to motion existing prior to inhalation. All responded to the inhalation with the immediate, transient, measurable and significant decrease in limitation indicated. A subjective impression of decrease in pain was reported, following first inhalation of CO_2, by all of the group but one. It could be corroborated by observation, before and after inhalation, of the amount of passive flexion or pressure required to elicit the painful sensation in question, in only 6. The effect on pain, like the effect on limitation of motion, was not observed following inhalation of oxygen unmixed with CO_2 but was more certainly elicited by mixtures of CO_2 with oxygen than by mixtures of CO_2 with air. Both effects persisted longest in those of the subjects making greatest effort to guard against over-breathing through self-control, stimulation of CO_2-production through persevering, mild, non-painful exercise, and precaution against chilling. Cumulative effect, following repeated inhalation, was obtained only up to the point of limitation by factors other than muscle spasm and pain.

Carbon dioxide was less certain and definite in effect on the conditions grouped in Table II.

Administration of 10 to 20% CO_2 in oxygen to rabbits was followed by the transient decrease in responsiveness to the stimulus of chilling[1] indicated in Fig. 1 and the associated[2] transient decrease in

[1] Locke, A., *J. Immunol.*, 1939, **36**, 159. 365.

[2] Locke, A., and Main, E. R., *J. Immunol.*, 1939, **36**, 173.

TABLE I.

Transient Decrease in Limitation to Movement Imposed by Muscle Spasm and Pain, in Rheumatoid (Atrophic) Arthritis, Following Inhalation of 10 to 15% CO_2.

Subject	No. of consecutive daily inhalations given	Extent of freedom permitted in the movement described	Before CO_2 inhalation	After	Indication of a decrease in pain as appraised by: Subject	Observer	Hr. duration of the combined effect
DB	1	Active flexion, knee	80°	complete	+	+	10
BB	1	" " knees	0°	0°			
	8			15,20°			
	14			15,20°			
	1	Upward motion, from bed: shoulders, elbows, heels	0 in.	3;1,6;0 in.	+	+	6-12
	8			4;6,10;4 in.			>12
	14			6;7,10;5,7 in.			retained
MC	1	Active flexion, left elbow	5°	10°			
	6			30°			
	34			40°			
	1	" " right knee	10°	10°	+	+	2
	16			20°			6-12
	34			35°			retained
	1	Raising right arm	110°	170°			
	1	Separation, teeth	¼ in.	¼ in.	(unable to eat solid food)		
	6			½ in.	(eating solid food)		
EW	1	Passive flexion, knees	40,50°	50,60°	+		6-12
LD	1	" " left elbow	0°	8°	+	+	1- 2
JP	1	Clenching hand	partial	complete	+		8
HG	1	Walking	limps	still limps	+		
	8		walking normally		+		
DN	1	Motility of arms and shoulders increased			+	+	6
VW	1	Motility of fingers increased			+	+	6-12
RF	1	" " " "					

TABLE II.

A Related but Less Frequently Elicited, Less Definite and Less Specific Effect in Conditions with Joint Stiffness, Pain or Incapacitation not Caused by Rheumatoid (Atrophic) Arthritis.

Subject	No. of consecutive daily inhalations given	Extent of freedom permitted in the movement described:	Before CO_2 inhalation	After	Indication of a decrease in pain as appraised by: Subject	Observer	Hr. duration of the combined effect
Osteo-arthritis:							
CB	1	Sitting up	to 60°	to 90°	+	+	6-12
NC	1	Passive flexion, knees	120,125°	130,137°			
PM	1	No measurable change			+		1
AR	1	" " "			+		6-12
Fibrositis:							
EM	1	" " "			+	+	1
EC	1	" " "					
OL	L	" " "			+		<1
Arthroplasty, post-operative:							
CA	1	Active flexion, elbow	0°	15°	+		7
E. coli Infection:							
CT	1	Motility of legs increased			+	+	3-4
Charcot Knee:							
MB	1	Ascending stairs	0	0	+	+	3-4
	7			+			>12

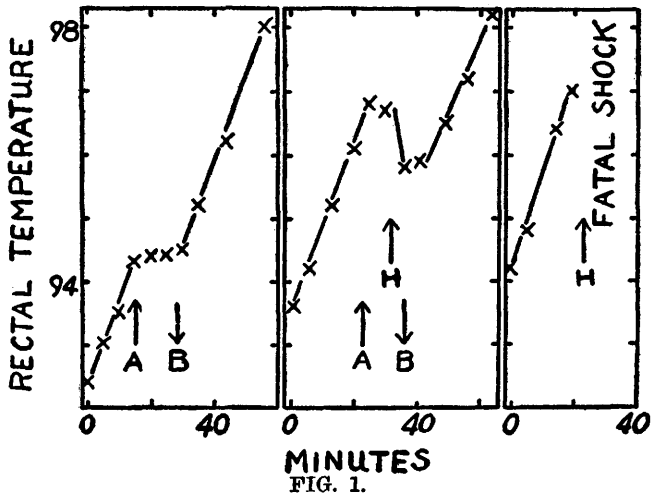

FIG. 1.

Effect of inhaled 10% CO_2 (in O_2) on responsiveness to stimulus and on susceptibility to histamine shock in chilled rabbits. The crosses indicate the course of spontaneous temperature recovery following chilling to the beginning temperatures indicated. A marks the time at which inhalation was begun; B marks the time of discontinuance; 0.8 mg of histamine was given, intravenously, at the time marked H.

susceptibility to histamine. Carbon dioxide raises the threshold of sensitivity to stimulus[3] to an extent capable of producing anesthesia[4] on inhalation for 1 minute or longer in concentrations exceeding 20%. Histamine is the possible chemical mediator of pain.[5]

Mixtures of carbon dioxide with air or oxygen have been given over long periods of time in amounts and concentrations in excess of those given the subjects in Tables I and II, without ill effect and with many indications of beneficial effect (improvement in peripheral circulation).[6, 7] Marked relaxation was observed by Loevenhart,[8] during administration of CO_2 to a group of psychotics for the purpose of rousing them from catatonia. Spontaneous movements of the extremities occurred. The eyes lost their fixed, staring quality and undertook purposeful movement. Carbon dioxide was given by Henderson[6] for the purpose of obtaining increase in collateral circulation in angina pectoris and intermittent claudication. Un-

3 Hettwer, J. P., *Am. J. Physiol.*, 1938, **122**, 275.

4 Leake, C. D., and Waters, R. M., *J. Pharm. and Exp. Therap.*, 1928, **33**, 280.

5 Rosenthal, S. R., and Minard, D., *J. Exp. Med.*, 1939, **70**, 415.

6 Henderson, Y., *Am. Heart J.*, 1930-31, **6**, 548.

7 Dautrebande, L., *et al.*, *Ann. physiol. physicochim. biol.*, 1938, **14**, 516; Klingman, T., *Ann. Int. Med.*, 1939, **13**, 677.

8 Loevenhart, A. S., Lorenz, W. F., and Waters, R. M., *J. Am. Med. Assn.*, 1929, **92**, 880.

mistakable increase in exercise tolerance was obtained. Kerr[9] and associates have used CO_2 to combat anxiety complex, effort syndrome and related conditions precipitated by hyperventilation and characterized by impaired ability to relax and to utilize relaxation as a means of conserving and accumulating strength. Over-breathing is a constant hazard when pain[10] is combined with inactivity. Maintenance of an adequate circulation is the major defense not only against low-grade infection[1] but also against atrophy and the type of structural change associated with arthritis.[11]

The observations reported above suggest, but do not establish, the possibility that CO_2-impoverishment may be a factor in the development and progress of atrophic arthritis. Work is under way on the larger problem of therapy. No conclusive progress in that direction has been obtained or is herewith implied.

Summary. A transient, small but measurable and significant decrease in limitation to motion was observed in 10 persons with atrophic arthritis following inhalation of 10 to 15% CO_2 (in O_2) for a length of time (2 to 5 min) sufficient to induce a feeling of warmth and breathlessness. An equivalently definite and regularly elicited effect was not observed in 10 additional persons with limitations due to conditions (osteo-arthritis, fibrositis, etc.) not classifiable as atrophic arthritis. Transient decrease in sensitivity to cold and in susceptibility to histamine was observed in rabbits during inhalation of CO_2 in O_2.

[9] Kerr, W. J., Dalton, J. W., and Gliebe, P. A., *Ann. Int. Med.*, 1937, **11**, 961; Soley, M. H., and Shock, N. W., *Am. J. Med. Sci.*, 1938, **196**, 840.

[10] Henderson, Y., *Am. J. Physiol.*, 1909-10, **25**, 310.

[11] Goldhaft, A. D., Wright, L. M., and Pemberton, R., *Am. J. Med. Sci.*, 1930, **180**, 386.