

to the increased cardiac work we would expect conditions in the arm to be unaffected and therefore the points on the graph to be scattered along the median curve DD. The fact, however, that the points representing these cases tend to approach the right hand edge (BC) of the curved area indicates, unexpectedly, that the oxygen consumption in the arm is also augmented and that probably the increased metabolism is general.

Conclusions. 1. Since pulse pressure $\times$ pulse rate $\times$ arterio-venous oxygen difference in the arms of different subjects roughly equals a constant, PP $\times$ PR is regarded as a fair index of blood flow entering the arm.

2. Since PP $\times$ PR is increased and A-V O₂ diff. is diminished in arterial hypertension and in certain anemias (in both of which total cardiac output is not increased), it follows that a larger proportion than normal of total blood flows through the arms (and possibly all limbs), *i. e.*, in these two conditions peripheral vasoconstriction is less marked in the arms than in the splanchnic area.

3. In hyperthyroidism the points on the graph are moved to the right of the normal curve indicating an increased oxygen use in the arm. The fact that many cases involving increased cardiac work also move to the right show that the increased metabolism in these cases is not due to increased cardiac work alone, but takes place in the arms also and is possibly a general condition.

4. It is suggested that the pulse pressure serves as a rough but valuable indication of the reciprocally varying needs and blood supply of the viscera and muscular masses of the body.

We are indebted to Dr. W. B. Porter, Professor of Medicine, for allowing us to make use of his clinical data.

13369

Acute Effects of Smoking on Respiration and Circulation.

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During experiments on the diurnal variations of alveolar CO₂ in man, the question arose as to whether smoking could be permitted occasionally, for it is often a hardship for the subject to refrain from smoking when no good evidence is available to contraindicate

it. I therefore studied the effects of smoking one cigaret on alveolar CO_2 , blood pressure, and heart rate of humans.

The subjects were 6 males in their early twenties. Some of these were smokers, averaging 20 cigarets a day, and the others were relative non-smokers, averaging not more than one or 2 cigarets a day. Complete non-smokers usually have difficulty inhaling smoke and were, therefore, not used. The subjects refrained from smoking, severe exercise and caffeine beverages for at least 3 hours previous to the experiment. Soon after their previous meal of breakfast or lunch, they lay down for from one-half to one hour, since at least 20 minutes is required to attain respiratory equilibrium,¹ until blood pressure and heart rate become constant. They remained supine during the entire experiment. The experiments were terminated before hunger contractions previous to the next meal appeared, to avoid their disturbance of alveolar CO_2 .² The alveolar CO_2 samples were obtained by the usual Haldane-Priestly technic, using the expiratory sample only. Samples were taken at 10- or 15-minute intervals, except immediately after smoking, when they were taken at intervals of from 1 to 3 minutes, in order to record more accurately the rapidly changing tensions. Blood pressure and heart rate determinations were made at 10-minute intervals except that following smoking they were taken at 5-minute intervals until the values were approaching normal.

To obtain quantitative results, the cigaret was marked with a pencil 23 mm from the mouth end and smoking ceased as soon as the fire reached this point. Although one puff a minute is considered average, I had the subjects take one puff every half minute, inhaling each one deeply, and attempting to inhale at the same depth each time, unless beginning to experience vertigo, when they were allowed to inhale somewhat less deeply. Thus the effects are exaggerated as compared to normal smoking. No attempt was made to determine what variations occurred in depth of inhalation between various individuals. The regular cigarets used were a leading brand containing 2% nicotine, each cigaret weighing 1 g.

As Fig. 1 shows, smoking one cigaret, using the above exaggerated technic, produces a distinct drop in alveolar CO_2 tension and a rise in blood pressure and heart rate. The effects are rather constant in any one individual, but vary considerably between subjects. Oddly, relative non-smokers do not always show a greater effect than smokers, and may show less. This may be due in part to differences

¹ Soley, M. H., and Shoen, N. W., *Am. J. Physiol.*, 1940, **130**, 771.

² Main, R. J., *Am. J. Physiol.*, 1937, **119**, 7.

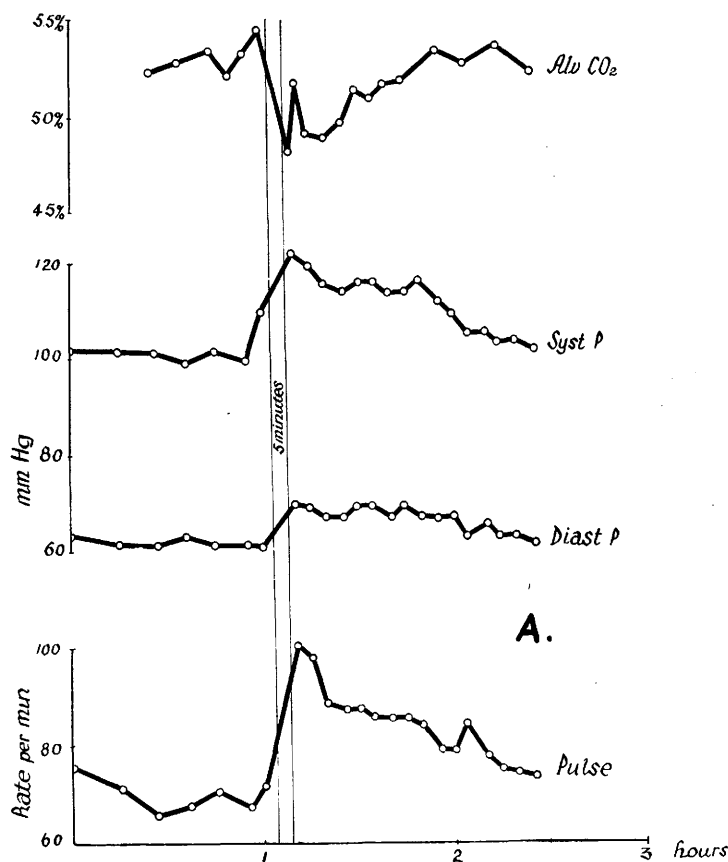


FIG. 1.

A. Response of subject F.L., a smoker, to a regular cigaret. B. Response of subject G.T., a relative non-smoker, to a regular cigaret. C. Response of subject F.L., to a denicotinized followed by a regular cigaret.

The vertical bar represents the duration of smoking.

The time in minutes written vertically on the bar represents the time required to smoke the cigaret.

in amount of smoke inhaled and the time it remains in the lung, or to individual sensitivity. The results indicate that the alveolar CO_2 is depressed for from 10 to 30 minutes following smoking, but that blood pressure and heart rate may not return to normal for from 30 to 60 minutes. These effects are much longer lasting than would be expected from the rapid detoxication of nicotine in rabbits³ but agree with the results in dogs.⁴ These results demonstrate the inadvisability of permitting smoking shortly before or during certain types of physiological experimentation.

³ Weatherby, J. H., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **42**, 593.

⁴ Biebl, M., Essex, H. E., and Mann, F. C., *Am. J. Physiol.*, 1932, **100**, 167.

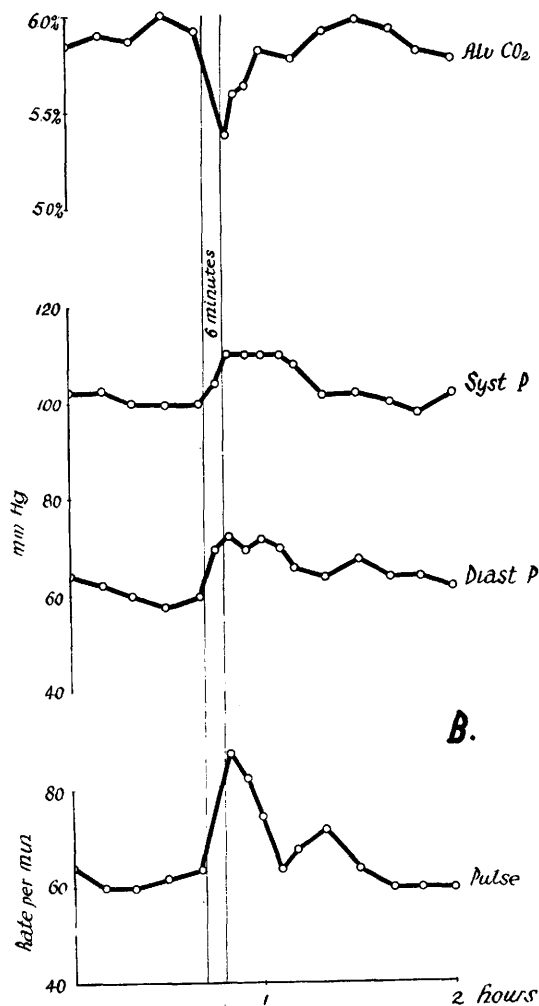


FIG. 1-B.

It then became of interest to determine the nature of the pharmacologic agent responsible for these physiologic disturbances. The substances in cigaret smoke most likely responsible are nicotine, CO, and irritating chemicals. Since nicotine seemed the most logical choice, some completely nicotine-free cigaretts of the same brand were made according to the technic to be reported by Weatherby.⁵ These cigaretts were then tested in the usual manner on 3 of the above subjects. The results (C, Fig. 1) indicate only a negligible effect on respiration and circulation, as compared to a regular cigaret.

⁵ Weatherby, J. H., unpublished data.

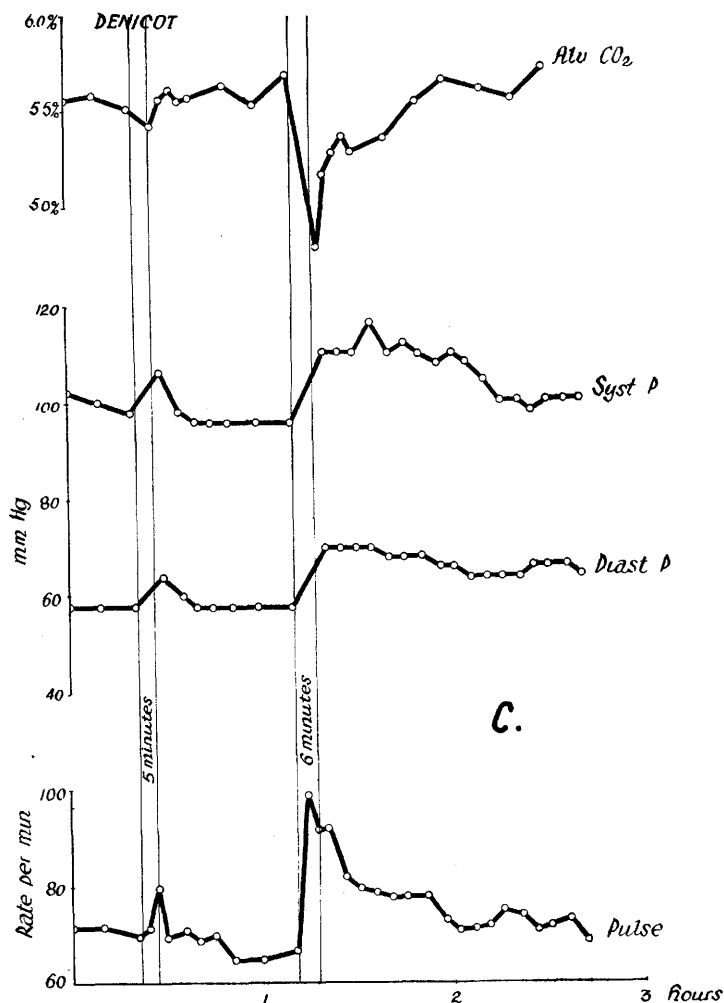


FIG. 1-C.

The effects passed off so quickly that for purposes of comparison, as soon as the subject returned to normal, he would smoke a regular cigaret, as indicated in the figure, (C, Fig. 1). Consequently, I conclude that nicotine is the chief pharmacologic agent in cigarets producing the effects described.

Since it has been suggested⁶ that the effect of smoking may be due to nicotine liberating epinephrine from the adrenals, it is of interest to point out that subcutaneously at least, and for an equivalent increase in blood pressure, epinephrine did not produce nearly so

⁶ Short, J. J., and Johnson, H. J., *J. Lab. and Clin. Med.*, 1938-39, **24**, 590.

marked a tachycardia and had no effect on alveolar CO₂ tension.⁷

Summary. Smoking one cigaret according to a standardized exaggerated technic, lowers alveolar CO₂ for from 10 to 30 minutes, and increases blood pressure and heart rate for from 30 to 60 minutes in both smokers and relative non-smokers. Nicotine-free ciga­rets produce very much less effect.

13370 P

Effects of Transplanted Blastemas on Amputated Nerveless Limbs of Urodele Larvae.

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(Introduced by O. C. Glaser.)

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Recent histological studies on early stages of Urodele regeneration have revealed that one of the primary consequences of limb amputation is the initiation of dedifferentiation at the amputation level. (Butler,^{1, 2} Puckett,³ and Thornton.^{4, 5}) It has been proposed by these authors that dedifferentiated cells contribute to the establishment of the regeneration blastema. The appearance of the blastema coincides with the cessation of dedifferentiation and marks the beginning of the regenerative processes.

Experimental evidence thus far presented indicates that an equilibrium of cellular interaction underlies regenerative activity. In particular, it has been suggested by Butler and Puckett⁶ that the blastema is important, not only in the establishment of a regenerate, but also in maintaining a balance between early dedifferentiation and later differentiation. When, by means of either X rays or ultraviolet light, regeneration is prevented, an active blastema never forms. Under such a condition the limb undergoes excessive dedifferentiation. Similar results have recently been obtained by Schotté and

⁷ Main, R. J., *Proc. Soc. Exp. Biol. and Med.*, 1940, **45**, 776.

¹ Butler, E. G., *J. Exp. Zool.*, 1933, **65**, 271.

² Butler, E. G., *Anat. Rec.*, 1935, **62**, 295.

³ Puckett, W. O., *J. Morph.*, 1936, **59**, 173.

⁴ Thornton, C. S., *J. Morph.*, 1938a, **62**, 17.

⁵ Thornton, C. S., *J. Morph.*, 1938b, **62**, 219.

⁶ Butler, E. G., and Puckett, W. O., *J. Exp. Zool.*, 1940, **84**, 223.