ATROPINE CIGARETTES IN ASTHMA AND EMPHYSEMA

BY

H. HERXHEIMER, M.D., L.R.C.P.&S.Ed.
Professor of Medicine in the Free University of Berlin; from the Department of Allergology

Before the advent of adrenaline as the main agent for immediate relief from an acute attack many asthmatics relied on burning a powder made from leaves of stramonium, belladonna, and/or hyoscyamus and inhaling the smoke. This was said to bring relief in some cases. This remedy is no longer in official use, although in Germany, for instance, "asthma cigarettes" consisting of powdered stramonium leaves can be bought in every chemist's shop, and it may be assumed that they are widely used without medical prescription. Current textbooks of pharmacology hardly mention atropine and hyoscyamine, the active principles in these powders, in the treatment of asthma.

One reason for this apparent neglect may be the observation that atropine given systemically has no appreciable effect in asthma. Locally, it is still used in aerosols, usually as atropine methonitrate, which is found in a concentration of 0.1% in the *British National Formulary* preparation of neb. adrenal. atrop. co. and in neb. isoprenal. co. as well as in many proprietary aerosol solutions. It is doubtful whether it has any anti-asthmatic effect in these preparations. I have not observed any benefit in patients using atropine methonitrate 0.1% as an aerosol (unpublished observations). If these preparations are inhaled frequently, however, they cause dryness of the mucous membranes. Their therapeutic inefficacy has also been mentioned by Wolfer (1956). This apparent discrepancy between the effects of wet atropine aerosol and atropine smoke made it desirable to reinvestigate the problem. This paper is concerned with the effect of *atropine smoke* on lung function in asthmatic and emphysematous patients.

Method

As the amount of atropine and hyoscyamine in commercial stramonium cigarettes is likely to vary, atropine cigarettes were prepared by the method of Holmstedt and Wallén (1959). Tobacco containing little nicotine (less than 0.06%) was used, and amounts of atropine sulphate were added which on burning the tobacco in the main stream,* according to the authors, left a residue of atropine in cigarettes of two different strengths, so that either 0.5 mg. or 1.45 mg. was inhaled by the patient. The patients were instructed to hold their breath after inhalation for at least two or three seconds. According to Baumberger (1923) and Ervenius *et al.* (1958) a much higher proportion of smoke particles is retained with this method than with ordinary breathing. Baumberger found that with ordinary "puffing" 67% was retained and with inhaling 88%; Ervenius *et al.* found that with "superficial" smoking 19% was retained and with inhaling 80%.

The rhythm of the smoking and the total time required for one cigarette were left to the patient, except that he was instructed not to hurry. The vital capacity (V.C.) was used as test of lung function. This method has stood the test of time, and in my opinion is as good an indicator of bronchial obstruction as any of the more fashionable methods, as, for instance, the timed V.C. and the M.B.C. (maximum breathing capacity). The latter methods have, particularly in asthmatics, the great disadvantage of increasing bronchial obstruction either by hyperventilation or by forced expiration from the maximum inspiration point. Many of our subjects acquired such a skill in breathing with the recording spirometer that their basal values varied only within a range of 50 ml. Such uniform results can be achieved only if enough time is allowed between estimations (in emphysematous subjects one and a half to two minutes) and if expiration from maximum inspiration point is avoided.

The patients taking part in the present investigations suffered from bronchial asthma or from emphysema. As is well known, long-standing bronchial asthma leads to a state of hyperinflation of the lungs commonly regarded as equivalent to emphysema. In this study the term "bronchial asthma" denotes chronic bronchial asthma of allergic or infective origin, whilst by emphysema is meant increasing breathlessness on exercise beginning with or without cough and proceeding (with rare exceptions) to moderate or severe incapacity from dyspnoea and bronchitis with hypersecretion, without primary heart disorder. Whether anatomical emphysema was present in any of these cases is uncertain. It is certain that bronchial obstruction and hyperinflation were present in all of them and that the hyperinflation was somewhat less reversible in the cases labelled emphysema.

Twenty-three subjects were tested with 1.45-mg. atropine cigarettes in 48 experiments, and 16 with 0.5-mg. cigarettes in 24 experiments. Ten patients were tested with both kinds of cigarettes. The procedure was as follows. The V.C. was recorded, in the sitting position, with a low-resistance spirometer and constant oxygen replacement, so that the tracing of the tidal air remained horizontal. The subject was asked to exhale as much as possible and then to resume normal breathing. After a few further normal breaths maximum inspiration was recorded. This procedure in most cases avoids the distension phenomenon first described by Christie and McIntosh (1934). This is a decrease of the V.C. caused by additional bronchial obstruction due to the high intrathoracic pressure resulting from the patient's pressing out from the maximum inspiration point.

When the patient had been trained in this method of recording the V.C. three recordings were taken. If they did not differ by more than 150 ml. their mean was used as the baseline; if they did, the highest reading was used, or the two highest if these were not more than 150 ml. apart. The subject then smoked the cigarette. The V.C. was again recorded three times: immediately after the cigarette had been smoked; again 10 to 15 minutes later; and then at varying intervals, in a few cases up to several hours. In some cases, particularly in those in which the V.C. increased to an unexpected degree after the cigarettes, the subject was on a later occasion, as a blind control, given a cigarette of the same kind without atropine.

In some further experiments ordinary commercially available asthma cigarettes were smoked which contained, according to the declaration of the manufacturers, nothing but folia stramonii. In other experiments a 0.5% solution of atropine sulphate with a

*"Main stream" smoke is the smoke which is inhaled by the smoker, in contrast to the smoke leaving the cigarette between the puffs.

little glycerin added was aerolized by the scrubber nebulizer of Dautrebande (1951), which, according to this author, delivers homogeneous aerosols of a particle size of 200–400 Å. The subject took 20 deep breaths of this aerosol, which was nebulized at a pressure of 0.3 atmosphere; this took about 3 minutes. It was observed that the amount of fluid lost from the scrubber during this procedure was about 150 mg., containing 0.75 mg. of atropine. Only a part of this amount is retained by the subject, as some of the aerosol is deposited in the tubes leading to the mouthpiece, and some of it is inhaled and exhaled again. If it is assumed that the subject has retained less than half of the total produced by the scrubber, this would be about 0.3 mg. of atropine.

As a comparison, a commercial nebulizer was used to produce a 0.5% atropine sulphate aerosol with a varying droplet size and a mean diameter of 2μ. The inhalation of this aerosol for 10–30 seconds had proved ineffective several years ago; in the present experiments it was used for periods up to three minutes.

Results

The results are given in Table I. In the great majority of cases the V.C. increased after the smoking, often by a substantial amount. This increase varied considerably. It was absent or negligible only in those cases in which the basal value was normal at the time of the experiment—that is, where the clinical condition of the patient was satisfactory and where it was not possible to increase the V.C. by other means (isoprenaline or ephedrine). Under those circumstances a further increase of the V.C. could not be expected from atropine (or from any other drug); these cases have been included in Table I, but not in our evaluation of the atropine effect. The increases of the other experiments range from 5% to 48%, and in 52 of the 62 experiments evaluated the increase was 10% or more. We have arbitrarily assumed increases from 5% to 9% to be "negative," although some of the small increases may well represent an atropine effect. Blank cigarettes did not change the V.C. more than ±3%. A decrease of the V.C. occurred in only two patients in whom the smoke induced cough with a subsequent fall of the V.C., from which they slowly recovered. These experiments have been omitted from Table I.

The increase often became noticeable immediately after the smoking—that is, after three to five minutes—but in only five of the experiments was the maximum increase reached at that time. In most cases (26) the maximum increase was reached after 15 to 30 minutes, in 14 experiments after 35 to 60 minutes. In seven experiments the maximum increase occurred only after one hour. The highest increase after 1.45 mg. atropine was 48%, after 0.5 mg. 34%. There were six "negative" results with 0.5 mg. and four with 1.45 mg. Both atropine doses were given to six patients (Table II). In all of them 1.45 mg. of atropine had a slightly but definitely stronger effect than 0.5 mg., the mean increase of the V.C. being 17% against 12%. The average maximum increase in all experiments, however, was equal for both doses (about 18%). In many cases the patients commented spontaneously on their increased ease of breathing.

The duration of the increase, which varied considerably, is shown in Figs. 1 and 2. At 90 minutes the increase was fully maintained, but after three hours it had mostly disappeared. In Fig. 1 an experiment with a maximum increase of 9% is included, as the time course of the increase and decrease of the V.C. is typical of an atropine effect.

TABLE I.—*Percentage Increase of Vital Capacity After Atropine Cigarettes*

Subj.	V.C. (cm.³) Before	Dose of Atropine (mg.)	Increase of V.C. after Minutes: 3–5	15–25	40–60	120	180	Remarks
Pl ..	2,505	1·45	6%	8%	16%			E
Pl ..	2,570	1·45	6%	13%	18%	(90') 0%		
Pl ..	2,485	1·45	11%	18%	16%			
Pl ..	2,440	1·45	10%	15%				
Pl ..	2,370	0·5	8%	14%				
Pl ..	2,215	0·5	6%					
Wi ..	3,550	1·45	0%	1%	6%	(95') 12%	(5 hr) 0%	E
Wi ..	*4,030	0·5	0%	—	0%			
Ed ..	*3,220	1·45	0%	0%	4%			E
Ed ..	2,820	0·5	7%	8%				
Teu ..	2,225	1·45	12%	20%				A
Teu ..	2,510	1·45	0%	10%	9%			
Teu ..	2,525	1·45	2%	10%				
Teu ..	*2,755	0·5	—	3%	3%			
Teu ..	2,580	0·5	3%	6%	10%			
Schie	*5,775	1·45	0%	0%				A
Kl ..	3,500	1·45	31%	34%	37%		(5½ hr.) 48%	A
Kl ..	5,360	1·45	13%	14%				(9 hr.) 0%
Els ..	2,455	1·45	8%	14%	26%	26%		E
Els ..	2,530	1·45	9%	12%	16%	(90') 17%		
Els ..	2,250	1·45	13%	20%	30%	16%	12%	
Els ..	2,120	1·45	18%	28%				
Gae ..	*4,230	1·45	0%	0%	0%	(100') 4%		A
Wol	2,560	1·45	26%	31%				E
Wol	2,875	1·45	16%	31%				
Wol	2,960	1·45	18%	20%				
Wol	3,170	1·45	11%	13%				
Wol	2,915	1·45	17%	30%	—	15%	17%	
Wol	2,875	1·45	18%	—	26%			
Wol	3,140	1·45	10%	13%		7%	4%	
Wol	2,975	0·5	9%	19%				
Wol	2,900	0·5	17%	—	25%			
Schwa	1,820	1·45	7%	—	5%	0%		E
Bel ..	1,920	1·45	5%	4%	0%			A
Bel ..	2,075	1·45	0%	9%	—	24%		
Bel ..	*3,100	1·45	0%	0%	—	(80') 0%		
Elix ..	2,640	1·45	3%		10%			A
Elix ..	1,400	0·5	34%	24%	33%			
Oberl	2,265	1·45	10%	—	13%			E
Oberl	2,175	0·5	—	0%	—	6%		
Mel ..	3,240	1·45	0%	0%	15%			A
Dr. Br	2,420	1·45	7%	5%	3%			E
Haut	*4,040	1·45	0%	0%				A
Pie ..	2,365	1·45	21%	28%				E
Pie ..	2,225	1·45	24%	29%				
Pie ..	2,040	1·45	19%	16%				
Pie ..	2,340	1·45	13%				(4 hr.) 0%	
Pie ..	1,895	0·5	10%	22%				
Pie ..	2,425	0·5	13%	15%				
Pie ..	2,225	0·5	11%	17%				
Pie ..	2,640	0·5	7%	—	15%			
Pie ..	2,425	1·45	12%	19%				
La ..	2,200	1·45	11%	28%				E
Wo ..	1,400	1·45	31%					E
Wo ..	1,770	1·45	21%	33%	—		(205') 19%	(8 hr.) 0%
Wo ..	2,035	1·45	13%	19%	(70') 20%	14%	(205') 22%	
Wo ..	1,710	1·45	10%	—	—	13%		
Ra ..	*3,035	1·45	0%	0%				A
Ra ..	*3,125	0·5	3%		0%			
Ra ..	2,605	1·45	9%	6%	—	3%		
Sk ..	1,745	1·45	14%	12%	—	(95') 14%	5%	E
Sk ..	1,790	0·5	—	6%	9%	(100') 6%	0%	
We ..	3,080	1·45	0%	—	14% 25%	(90') 13%		E
Dall	2,185	1·45	19%	—	18%			A
Qu ..	2,300	0·5	6%	—	12%	(85') 13%		E
Bross	3,555	0·5	3%	—	7%	5%		A
Ku ..	2,400	0·5	7%	—	0%			E
Kum	3,380	0·5	20%	27%				E
Lü ..	2,590	0·5	3%	19%				E
Lü ..	2,420	0·5	14%		23%			
Lü ..	*3,190	0·5	0%	2%				
Lin ..	1,730	0·5	0%	15%	23%		(165') 2%	E

*Normal basal value. E=Emphysema. A=Asthma. Values given between 2 adjacent columns were obtained at intermediate times.

In some experiments ephedrine was given first and the resulting increase of V.C. recorded. When it had reached what was assumed to be its peak an atropine cigarette was smoked in order to test whether this substance had an additional effect. In other experiments this order was reversed. The results (Table III) show that in many cases the V.C. increased after ephedrine and after atropine independently of the order in which they were given.

The results with cigarettes containing stramonium were similar to those with the atropine cigarettes (Table IV). The inhalation of the 0.5% wet atropine aerosol with the Dautrebande scrubber also caused an increase in V.C. (Table V). When this was compared with the effect of a 0.5% atropine aerosol from an ordinary commercial nebulizer, a one-minute continuous respiration showed an increase of the V.C. in three experiments, whilst there is very little change in the other two. When, in those two experiments, the subject smoked in addition an atropine cigarette the increase of the V.C. became substantial. When, however, in five other experiments the inhalation period was extended to three minutes, the increase in V.C. was substantial and comparable to that seen after inhaling from the scrubber and after atropine cigarettes (Table V).

TABLE II.—*Means of Greatest Increase in V.C. in Patients Who Had Both Doses of Atropine*

Subj.	0·5 mg.			1·45 mg.		
	No. of Obs.	Mean Initial V.C. (cm.³)	Mean Increase	No. of Obs.	Mean Initial V.C. (cm.³)	Mean Increase
Pl ..	2	2,300	10%	4	2,500	17%
Teu ..	1	2,580	10%	3	2,500	17%
Wol	2	2,940	22%	7	2,920	26%
Oberl	1	2,175	6%	1	2,265	10%
Pie	4	2,295	17%	5	2,280	22%
Sk ..	1	1,790	9%	1	1,745	14%

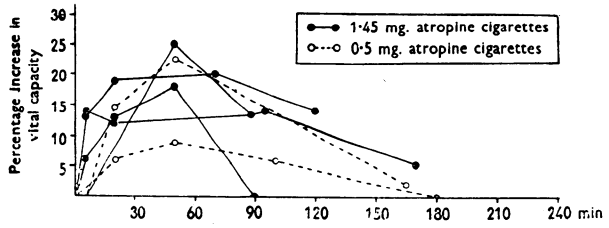

FIG. 1.—Duration of effect of atropine smoke on vital capacity.

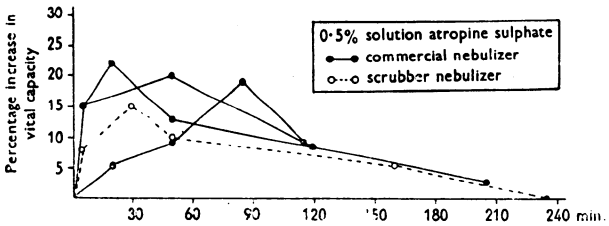

FIG. 2.—Duration of effect of atropine aerosol on vital capacity.

TABLE IV.—*Cigarettes with Folia Stramonii*

Subj.	V.C. (cm.³) Before	Doses	Increase of V.C. After ‡		
			3–5 min.	15–25 min.	30 min.
Wol ..	3,050	1 cig. stram.	9%	17%	
Ku ..	3,200	,, ,, ,,	17%	23%	
Pie ..	2,470	,, ,, ,,	15%	22%	
Lin ..	1,395	,, ,, ,,	8%	14%	
Pl ..	2,120	,, ,, ,,	14%	13%	
		*1 cig. atr. 1·45	18%	26%	
Pl ..	2,440	1 cig. atr. 1·45	11%	—	15%
		†1 cig. stram.	11%	—	19%

* This atropine cigarette was smoked 19 minutes after beginning the experiment.
† This stramonium cigarette was smoked 30 minutes after beginning the experiment.

Discussion

The present results leave no doubt that the inhalation of atropine smoke has a beneficial effect on lung function in bronchial obstruction. This effect is a little greater with 1.45 mg. than with 0.5 mg. and often lasts several hours; unpleasant side-effects, like cough, have been rare, although it is possible that they will increase with frequent use of this remedy. This positive result accords well with the animal experiments of Bouaziz (1954), who found that smoke containing atropine antagonized bronchial spasm induced by acetylcholine (though it was less potent in histamine-induced spasm). The present results show that the low esteem in which current textbooks hold atropine in the treatment of asthma is not justified and that atropine smoke has a definite place in the treatment of asthma and emphysema. This is important, because the therapeutic range of other available substances, particularly in emphysema, is limited. Ephedrine, the most valuable substance, becomes ineffective when given more than twice daily because tolerance develops (Herxheimer, 1946), and is contraindicated in the evening because of its central stimulant action. Moreover, it often has unpleasant side-effects. It is therefore most desirable to have a drug with an anti-spasmodic effect which lacks the disadvantages of ephedrine and can be given when ephedrine is contraindicated or in order to increase its effect.

The present results accord well with the reputation that stramonium enjoyed with the medical profession

TABLE III.—*Ephedrine and Atropine given in Succession*

Subj.	V.C. (cm.³) Before	Doses	V.C. After							
			3–5 min.	15–25 min.	40–60 min.	Doses*	73–75 min.	85–95 min.	110–130 min.	2 hr.
Quo†	1,990	75 mg. eph. oral	—	—	1,985	1 cig. atr. 1·45	2,285	2,275	2,420 2,340	
Quo†	2,120	125 ,, ,, ,,	—	—	(72') 2,100	1 ,, ,, 1·45	2,395	2,425	2,505	
Quo†	2,405	100 ,, ,, i.v.	2,355	—	2,325	1 ,, ,, 0·5	2,730	2,850		
Sk† ..	1,670	400 ,, methyleph. i.v.	1,620	—	1,610	1 ,, ,, 1·45	1,800	2,020		
Ed ..	2,705	1 cig. atr. 1·45 mg.	3,000	2,905	3,020 —	50 mg. eph. oral	—	—	3,040‡ 3,170 (90')	3,065
Kl ..	3,220	50 mg. eph. i.v.	4,430	—	4,820	1 cig. atr. 0·5	5,230	—	6,060	
Schw	1,780	75 mg. eph. oral and 50 mg. i.v.	1,890	1,975	—	1 ,, ,, 1·45	1,905	1,785	2,000	
Wol ..	2,810	100 mg. methyleph. i.v.	3,050	—	3,075 —	1 ,, ,, 1·45	3,600	—	—	
Lü ..	2,050	150 mg. eph. i.v.	2,420	—	—	1 ,, ,, 1·45	2,460	2,590		
Pl ..	1,995	760 mg. methyleph. oral	—	—	2,195	1 ,, ,, 0·5	2,440	—	—	
Lin ..	1,420	50 mg. eph. oral	—	—	1,555	1 ,, ,, 1·45	1,570	1,860		
Ra ..	2,060	100 ,, ,, ,,	—	—	2,590	1 ,, ,, 1·45	2,735	2,765	2,780	
Pie	1,880	1 cig. atr. 0·5	2,100	—	2,045 —	120 mg. methyl eph. i.v.	2,420			
Lan	2,120	1 ,, ,, 0·5	2,650	—	3,070 —	50 mg. eph. i.v.	3,000	3,160		

*The second drug was given 60-70 minutes after the first. † This subject was refractory to ephedrine. ‡ Close to the normal V.C. of this subject.

TABLE V.—*Effect of Wet 0.5% Atropine Aerosols From Scrubber Nebulizer and Commercial Nebulizer*

Subj.	V.C. (cm.³) Before	Doses	Increase of V.C. After				
			3–5 min.	15–25 min.	40–60 min.	2 hr.	3 hr.
Wo ..	1,815	20 deep breaths 0·5 atropine scrubber nebulizer	15%	22%	13%	(135') 7%	
Pie ..	2,560	,, ,, ,,	9%	12%	(70') 11%		
Pl ..	2,320	,, ,, ,,	15%	—	20%	8%	
Wol	3,110	,, ,, ,,	13%	18%			
Sk ..	1,825	,, ,, ,,	—	5%	8%	(85') 19%	
Tre ..	1,850	,, ,, ,,	—	6%	2%		
Haus	2,400	,, ,, ,,	0%	12%			
Ra ..	2,675	2×12 deep breaths 0·5% atr. scrubber nebulizer	7%	13%			
Pie ..	2,360	1 min. 0·5% atr. comm. nebul.	8%	15%	10%		(165') 5%
Wol*	3,015	1 min. 0·5% atr. comm. nebul.	5%	7%	4%		
		60 min. later 1 cig. atr. 1·45	15%	18%		11%	
Sk* ..	1,745	1 min. 0·5% atr. comm. nebul.	5%	—	0%		
		60 min. later 1 cig. atr. 1·45	14%	12%	—	(95') 14%	
Pl ..	2,590	3 min. 0·5% atr. comm. nebul.	7%	14%			
We ..	3,300	,, ,, ,,	5%	—	22%		
Kum ..	3,795	,, ,, ,,	10%				
Sk ..	1,565	,, ,, ,,	14%	2%	4%		
Wo ..	1,560	,, ,, ,,	19%	17%			

* Smoked an atropine cigarette 60 minutes after having the wet aerosol.

100 to 150 years ago. It is a matter for conjecture why it has since fallen into disrepute. Finnegan (1950) has given a detailed review of this development. It appears that the use of stramonium leaves in Europe dates back to the beginning of the nineteenth century. Favourable reports were published in 1811 and in the years that followed (Christie, 1811; English, 1811; Hageweisch, 1813; Miquel, 1836; Mirande, 1837; and others). Between 1890 and 1930 the literature does not seem to mention stramonium as a valuable remedy.

More recently, with the appearance of many textbooks of allergology, varied opinions have been expressed, although mostly with little supporting evidence. Thus Walzer (1931), Rackemann (1931), Vaughan (1934), Crisp (1945), and Cooke (1947), mention stramonium powder as a beneficial drug, though in a rather non-committal way, whereas Rowe (1937), Feinberg (1934), Bray (1934), Tuft (1937), Unger (1945), Urbach and Gottlieb (1946), Carryer *et al.* (1946), and Alexander (1947) are critical of its use. The latter authors think that the repeated use causes irritation of the air passages, and some of them attribute the beneficial effect mainly to the potassium nitrate often mixed with powdered stramonium leaves. Moreover, Swineford (1937) observed a case of asthma in which sensitivity to the powder had developed during the five years of its continued use. This critical attitude does not seem fully justified. If indeed such side-effects should occur through continued use of atropine smoke, its use must be restricted accordingly. But even its restricted use seems to be a valuable addition to the group of therapeutically effective substances.

The beneficial effect is, of course, not limited to atropine cigarettes: it occurs, for the same pharmacological reasons, with cigarettes made from stramonium leaves and also with wet atropine aerosols, provided that the droplets are small enough to penetrate into the finer bronchioli. It is probable that the very small particle size which permits penetration into the alveolar ducts and possibly into the alveoli is essential for the beneficial effect of the atropine smoke as well as of the wet aerosols. The negative result of earlier observations with wet aerosols is probably explained by the smaller amount of atropine in the aerosol used and by the shorter duration of its application, possibly also by the preponderance of larger particles not able to penetrate into the finer air passages.

There are thus three different methods for the local application of atropine in very small particles: the stramonium cigarette, the atropine cigarette, and the wet aerosol. Compared with the first, the atropine cigarette has the advantage of presenting an accurately known dosage. The wet aerosol has the advantage that no irritation through other substances present in smoke can occur. Its practical disadvantage is that the apparatus for the production of such fine aerosols is a little cumbersome and cannot easily be used in daily life. The atropine cigarette, however, is easy to use, particularly if the tobacco employed as carrier is freed from irritating substances and has an inoffensive smell.

The dosage of atropine used in the present experiments requires comment. As the cigarettes producing 0.5 mg. of atropine had an effect similar to that of the stronger ones, it must be assumed that this amount was effective. As some of the smoke is exhaled by the patient, and as the retained particles, according to Ervenius *et al.* (1958) represent, with deep inhalation of the smoke, not more than 80% of the total main stream smoke, the effective amount of atropine appears to be less than 0.4 mg. How much less is not known, as the amount uselessly deposited in the upper respiratory passages is unknown. With the wet atropine aerosol, the total amount of atropine retained may be similar.

On the other hand, oral atropine in man has no effect in bronchial asthma even if it is given in amounts of 1 mg. It is probable that larger doses would be effective (Cullumbine *et al.*, 1955), but their side-effects limit their use. In the guinea-pig, which tolerates large amounts of atropine, high doses (Armitage *et al.*, 1952) have a certain protective effect against the anaphylactic microshock which closely resembles bronchial asthma; and in the isolated organ, the tracheal chain, atropine also counteracts bronchial spasm (Schild, 1936).

From this it appears that an effect can be achieved with very much smaller doses applied locally than by systemic administration. This local effect is achieved in the smaller bronchi, the alveolar ducts, or the alveoli themselves. Whether this is mediated through nervous elements or whether it is a direct effect on the bronchial muscle is not clear. It can hardly be a systemic effect: the small amount of effective substance points against it; moreover, the pulse rate in many of our subjects did not increase under the influence of the atropine smoke, and the maximum increase observed was six beats a minute. Mydriasis was not seen during the experiments (it may have appeared later), and only one subject complained of dryness of the mouth.

It is well known that the mechanism of action is different from that of ephedrine. I have seen cases in which large doses of ephedrine were quite ineffective, whereas atropine was effective, and in a number of

experiments (Table III) it has been shown that the effect of both substances is complementary.

Summary

Atropine administered locally in cigarette smoke or wet aerosols increases the vital capacity and gives a feeling of relief in cases of mild or moderate chronic asthma and emphysema.

The effective dose probably lies below 0.4 mg. of atropine sulphate.

Atropine is easily administered by smoking. This method of administration is simple; as the dosage can be accurately controlled, it is preferable to that of wet aerosols and of stramonium cigarettes.

I am indebted to Dr. B. Holmstedt, Stockholm, and Dr. Andrew Herxheimer, London, for their advice, and to the Vitrum Company, Stockholm, 12, which supplied the atropine cigarettes. Messrs. E. Merck & Co., Darmstadt, kindly supplied methylephedrine in tablets and solution.

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The Nutrition Research Laboratories of the Indian Council of Medical Research have just issued their annual report for 1957–8. Studies on proteins and protein malnutrition, iron metabolism, and vitamins are included. There are sections devoted to field investigations in some Nilgiri tribes; studies in human lactation; and the growth and physical development of Indian children. A brief account is given of the education and advisory work done by the Laboratories (*Annual Report for 1957–8*, Nutrition Research Laboratories, India Council of Medical Research).

TREATMENT OF PILONIDAL SINUS BY EXCISION AND PRIMARY CLOSURE*

BY

A. J. H. RAINS, M.S., F.R.C.S.
Surgeon, United Birmingham Hospitals

In the past seven years the cure of 442 cases of pilonidal sinus has been undertaken in the United Birmingham Hospitals, a teaching group where it is to be expected that a complete spectrum of cases and operations is to be seen besides operations of a highly specialized nature requiring team-work.

Except in those instances where the patient presents with an acute abscess for incision and drainage, the track and ramifications of the sinus must be excised. There are two opposing views on what should be done with the wound after this: should it be left open to be allowed to granulate from the bottom or be closed by primary suture? Textbook and practice have often given the impression that the former method is the one of choice on the grounds that the sinus is chronically infected, that the whole area is a "dirty" one, and that the frequent multiplicity of sinus openings prevents the surgeon from obtaining and retaining primary closure of the wound. A random sample of the records of 72 cases treated in one of the two teaching hospitals here shows that 33 wounds were allowed to granulate and 39 were closed by primary suture (46.5% : 53.5%).

If the wound is allowed to granulate, the patient must be resigned to a longer stay in hospital, time in a convalescent hospital, and an extended period off work, with daily dressings carried out by a district nurse. The open wound is unpleasant, the scar is liable to excoriation, and recurrence, for which the pilonidal sinus is notorious, is still possible. Of the 33 cases mentioned above, four recurred. Of the 39 cases of excision and closure, three recurred.

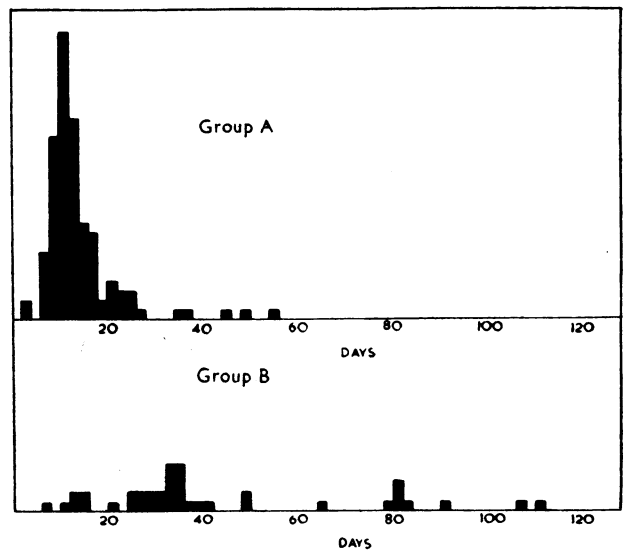

FIG. 1.—Number of days spent in hospital by patients. The majority of group A cases (after excision and primary suture) are sent home with wounds healed. The early discharges in group B patients are sent out of hospital with open wounds, which are dressed in a convalescent hospital or at home by a district nurse.

When careful attention is paid to technique, success from primary suture may nearly always be achieved

*Read to the Section of Surgery at the Annual Meeting of the British Medical Association, Birmingham, 1958.