

ALIMENTARY TRACT

Mechanisms of acid reflux associated with cigarette smoking

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Abstract

Studies were done to evaluate the lower oesophageal sphincter function of chronic smokers compared with non-smokers and to ascertain the acute effects of smoking on the sphincter and the occurrence of acid reflux. All subjects (non-smokers, asymptomatic cigarette smokers, and smokers with oesophagitis) were studied postprandially with a lower oesophageal sphincter sleeve assembly, distal oesophageal pH electrode, and submental electromyographic electrodes. The two groups of cigarette smokers then smoked three cigarettes in succession before being recorded for an additional hour. As a group, the cigarette smokers had significantly lower lower oesophageal sphincter pressure compared with non-smokers but the sphincter was not further compromised by acutely smoking cigarettes. Cigarette smoking did, however, acutely increase the rate at which acid reflux events occurred. The mechanisms of acid reflux during cigarette smoking were mainly dependent upon the coexistence of diminished lower oesophageal sphincter pressure. Fewer than half of reflux events occurred by transient lower oesophageal sphincter relaxations. The majority of acid reflux occurred with coughing or deep inspiration during which abrupt increases in intra-abdominal pressure overpowered a feeble sphincter. We conclude that cigarette smoking probably exacerbates reflux disease by directly provoking acid reflux and perhaps by a long lasting reduction of lower oesophageal sphincter pressure.

The role of cigarette smoking as an aggravating factor in the pathogenesis of gastro-oesophageal reflux disease is incompletely understood. That some association exists is suggested by the epidemiologic association between symptomatic reflux disease and cigarette smoking which has been reported as high as 92% in some series.¹ In a recent study, however, using 24-hour ambulatory oesophageal pH monitoring, Schindlbeck *et al* reported that despite the observation that as a group, smokers had more reflux episodes than non-smokers, neither the act of smoking nor the fact of being a smoker increased the oesophageal acid exposure time. These findings led the authors to conclude that, 'it is questionable whether abstaining from smoking has a beneficial effect in patients with reflux disease'.² On the other hand, other investigators had recorded

distal oesophageal pH in 25 smokers with reflux disease for 15 hours and found that of 226 reflux episodes recorded, 102 were associated with smoking a cigarette. Similarly, the reflux scores derived from standard acid reflux tests performed during smoking were significantly worse than scores for the same individuals while not smoking.¹ Another line of evidence suggesting cigarette smoking to be detrimental with respect to reflux disease comes from a therapeutic trial of the efficacy of ranitidine in healing peptic oesophagitis. In a study of 108 patients with peptic oesophagitis, about half of whom smoked, the amount that individuals smoked correlated directly with the likelihood of failure to heal lesions after six weeks of therapy.³

The effect of cigarette smoking on lower oesophageal sphincter pressure has been studied using oesophageal manometry and Dennish *et al* reported an acute reduction in lower oesophageal sphincter pressure during cigarette smoking. The period of decreased pressure was confined to the period of actual smoking and showed complete recovery within five minutes after cessation of smoking.⁴ Stanciu *et al* used similar methods and found smoking to diminish lower oesophageal sphincter pressure with complete recovery within three to eight minutes after the termination of smoking.¹ Pull-through techniques were used to measure the lower oesophageal sphincter pressure in both of these studies and it is unclear how this was accomplished while the subjects were actually puffing on a cigarette as that would seem to interfere with the pressure measurement. Most likely, smoking was temporarily suspended to allow for the pull-through. Thus, existing data suggest that during the act of cigarette smoking there is an acute reduction in lower oesophageal sphincter pressure and it is implied that the diminished lower oesophageal sphincter pressure results in acid reflux. Our present understanding of the mechanism by which acid reflux occurs, however, emphasises the importance of non-deglutitive transient lower oesophageal sphincter relaxations rather than the absolute value of lower oesophageal sphincter pressure.⁵⁻⁷ Long interval manometric studies of normal subjects suggest that 98% of acid reflux events occur in association with transient lower oesophageal sphincter relaxations while about 66% of reflux events in patients with oesophagitis are attributable to transient lower oesophageal sphincter relaxations. At present, data do not exist on the relationship between cigarette smoking and

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transient lower oesophageal sphincter relaxations.

The present work was undertaken to evaluate further the relationship of cigarette smoking to acid reflux events using manometric techniques that allow for continuous recording of lower oesophageal sphincter pressure and oesophageal motor activity concurrently with distal oesophageal pH recording. Specifically, experiments were designed to: (1) evaluate the lower oesophageal sphincter function of smokers with and without oesophagitis compared with that of non-smokers, (2) examine the acute effects of cigarette smoking on lower oesophageal sphincter function, and (3) evaluate the relationship of cigarette smoking to the occurrence and mechanism of gastro-oesophageal acid reflux.

Methods

SUBJECTS

Manometric studies were obtained on eight non-smoking volunteers (age 30 (five) years), nine cigarette smokers without symptoms referable to the oesophagus and a negative Bernstein test (age 33 (15) years), and nine patients with heartburn and oesophagitis demonstrated endoscopically within seven days of the study (age 63 (15) years). The admitted smoking histories of the subjects were 5.8 (4.4) thousand packs for the asymptomatic smokers and 19.3 (7.7) thousand packs for the smokers with oesophagitis. Of the subjects with oesophagitis, all had a sliding hiatal hernia, and all had either distal oesophageal erosions (n=six) or exudate and a mucosal biopsy showing either inflammatory cells or increased thickness of the basal cell layer (n=three). The study protocol was approved by the Institutional Review Board of Northwestern University.

Oesophageal pressure recordings were obtained with a manometric assembly incorporating a 6 cm sleeve sensor, four side-hole recording sites situated 0, 3, 6, and 9 cm from the proximal margin of the sleeve sensor, and a gastric recording site at the distal end of the sleeve sensor.^{8,9} Oesophageal pH recordings were obtained with a glass pH electrode (Cecar Microcombination pH Electrode, Beckman Instruments, Irvine, Calif). Submental electromyographic recordings were obtained using silver-silver chloride disc electrodes (Beckman) positioned under the chin and an indifferent electrolyte patch fastened to the side of the subject's neck. The electromyographic signal was processed by a high pass filter set at 5.3 Hz to minimise the movement artefact recorded. The manometric assembly and the pH electrode were passed transnasally into the oesophagus and the sleeve assembly was positioned with the sensing membrane axially centred in the lower oesophageal sphincter high pressure zone. The pH electrode was positioned 5 cm above the midpoint of the lower oesophageal sphincter. After placement, the manometric assembly and the pH electrode were taped securely to the patient's nose. Each lumen of the manometric assembly was perfused at 0.4 ml/min with a pneumohydraulic infusion pump¹⁰ and connected to a Gould-Statham 23DB pressure transducer (Gould Medical Products, Oxnard, Calif). The manometric recordings, pH recording, and

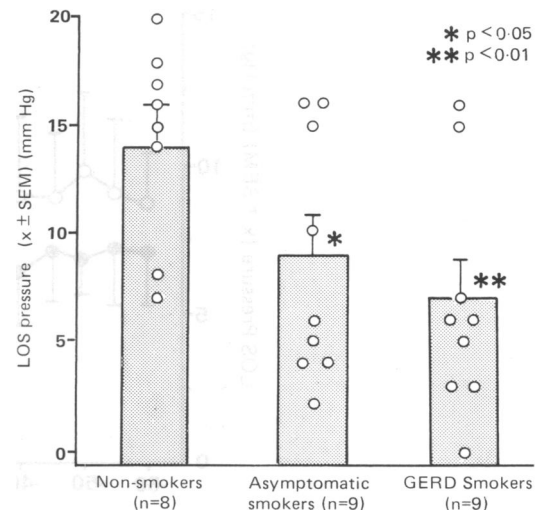


Figure 1: Mean lower oesophageal sphincter pressure for one hour of recording obtained one hour postprandial. The mean value for the non-smoking volunteers (14 mmHg) was significantly greater than that of the asymptomatic smokers (9 mmHg) or the smokers with reflux disease (7 mmHg). The open circles represent data points for individual subjects. Two of the non-smokers, five of the asymptomatic smokers and six of the smokers with reflux disease had postprandial lower oesophageal sphincter pressure values of less than 10 mmHg.

the electromyographic tracing were displayed on an eight channel polygraph (Sensormedics Corp, Anaheim, Calif).

Studies were conducted in the morning with the subjects lying supine. One hour before intubation, they consumed an 800 kcal, balanced meal. Subjects had not smoked for a minimum of six hours before the study. After intubation, and a 10–20 minute adaptation period, a one hour recording was obtained of oesophageal motor activity and oesophageal pH. The subjects in both smoking groups then smoked three cigarettes successively over a 20–30 minute period. All subjects smoked their usual brands. Recording was continued for one hour after the cessation of cigarette smoking. Throughout the recording session, the subject's activities (coughing, puffing, talking, moving, etc) were noted on the polygraph record.

Mean end-expiratory basal lower oesophageal sphincter pressure was determined for each five minute epoch with a digital planimeter (Planix 7, Leitz Electronics). The lower oesophageal sphincter pressure tracing during transient lower oesophageal sphincter relaxations, swallow related relaxations, post swallow contractions, or abdominal straining were not scored within these five minute epochs. Values of lower oesophageal sphincter pressure were referenced to intra-gastric pressure. Grand mean lower oesophageal sphincter pressure values were computed by averaging the values of the five minute epochs. The periods while subjects were smoking the three cigarettes successively were characterised by an increased swallowing rate, frequent coughing, and significant respiratory artifact making the corresponding lower oesophageal sphincter pressure tracings unsuitable for the accurate scoring of basal lower oesophageal sphincter pressure. In order to examine the acute effect of cigarette smoking on lower oesophageal sphincter pressure, the five minute epochs be-

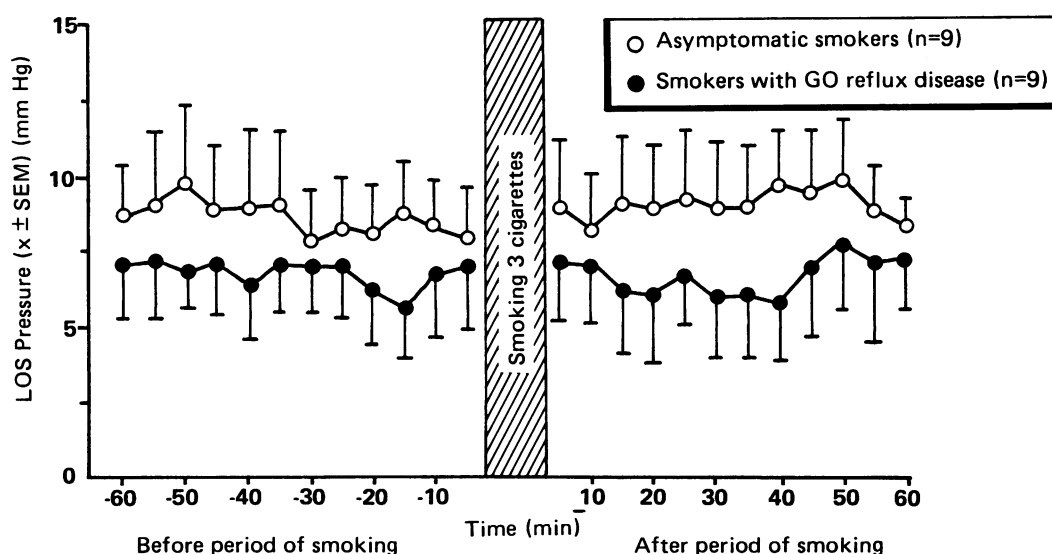


Figure 2: The acute effect of cigarette smoking on lower oesophageal sphincter pressure. Each data point represents the mean lower oesophageal sphincter pressure value for a five minute interval in the designated group of subjects. The lower oesophageal sphincter pressure was not significantly changed in either group after cigarette smoking. Although the group of smokers with reflux disease had consistently lower lower oesophageal sphincter pressure values than did the asymptomatic smokers, these differences did not achieve statistical significance.

fore and immediately after completion of the smoking period were divided into one minute periods, each of which was then analysed planimetrically. Transient lower oesophageal sphincter relaxations were scored by the following criteria: complete lower oesophageal sphincter relaxation to within 2 mmHg of gastric pressure persisting for a period of at least five seconds, decrease of lower oesophageal sphincter pressure of at least 5 mmHg, and the absence of submental electromyographic evidence of a swallow during the five seconds antecedent to the onset of lower oesophageal sphincter relaxation. Gastro-oesophageal acid reflux events were scored when the oesophageal pH decreased to a value of less than 4 for a period of at least five seconds.

All numerical data are expressed as mean (1) standard deviation unless otherwise specified. Statistical comparisons of data were done using either an analysis of variance as in the case of basal lower oesophageal sphincter pressure data or Student's *t* test for data sets in which two groups were being directly compared.

Results

LOWER OESOPHAGEAL SPHINCTER PRESSURE
The mean lower oesophageal sphincter pressure values for each of the three groups of subjects

obtained during one hour of baseline recording are illustrated in Figure 1. Note that, as a group, the asymptomatic smokers had significantly lower lower oesophageal sphincter pressure (9 (6) mmHg) than did the non-smokers (14 (5) mmHg) ($p < 0.05$) and that the smokers with reflux disease had a mean lower oesophageal sphincter pressure slightly lower yet (7 (5) mmHg) ($p < 0.01$). Inspection of the individual data points in Figure 1 suggests that actually each group of subjects was comprised of a subgroup of individuals with a lower oesophageal sphincter pressure of about 15 mmHg and another subgroup with a lower oesophageal sphincter pressure of less than 10 mmHg. The number of individuals in the subgroup with low lower oesophageal sphincter pressure values became progressively greater from the non-smokers (two of eight) to the asymptomatic smokers (five of nine) to the group of smokers with gastro-oesophageal reflux disease (seven of nine). Within the smoking groups, a correlation could not be found between the extent of the individuals smoking history and the numeric value of the lower oesophageal sphincter pressure.

The acute effect of cigarette smoking on lower oesophageal sphincter pressure was studied in both the group of asymptomatic smokers and in the group of smokers with reflux disease. Figure 2 shows the mean lower oesophageal sphincter pressure value during each five minute interval for each group of smokers. The lower oesophageal sphincter

TABLE Acute effect of smoking period on lower oesophageal sphincter pressure of asymptomatic smokers

Minute	Lower oesophageal sphincter pressure in mmHg									
	Immediately before smoking					Immediately after smoking				
	-5	-4	-3	-2	-1	1	2	3	4	5
Subject 1	22	21	18	16	19	10	12	18	13	15
Subject 2	7	7	11	11	12	16	20	21	12	14
Subject 3	4	2	2	1	6	5	8	5	1	2
Subject 4	9	7	7	1	4	4	3	1	1	1
Subject 5	8	6	7	7	5	4	6	7	6	6
Subject 6	3	4	5	3	9	10	5	7	7	4
Subject 7	7	5	9	11	9	11	7	6	8	6
Subject 8	10	12	10	8	8	19	14	28	28	22
Subject 9	11	8	9	3	5	3	8	4	3	4
Mean (SD)	9 (6)	8 (6)	9 (4)	7 (5)	9 (5)	9 (6)	9 (5)	11 (9)	9 (8)	8 (7)

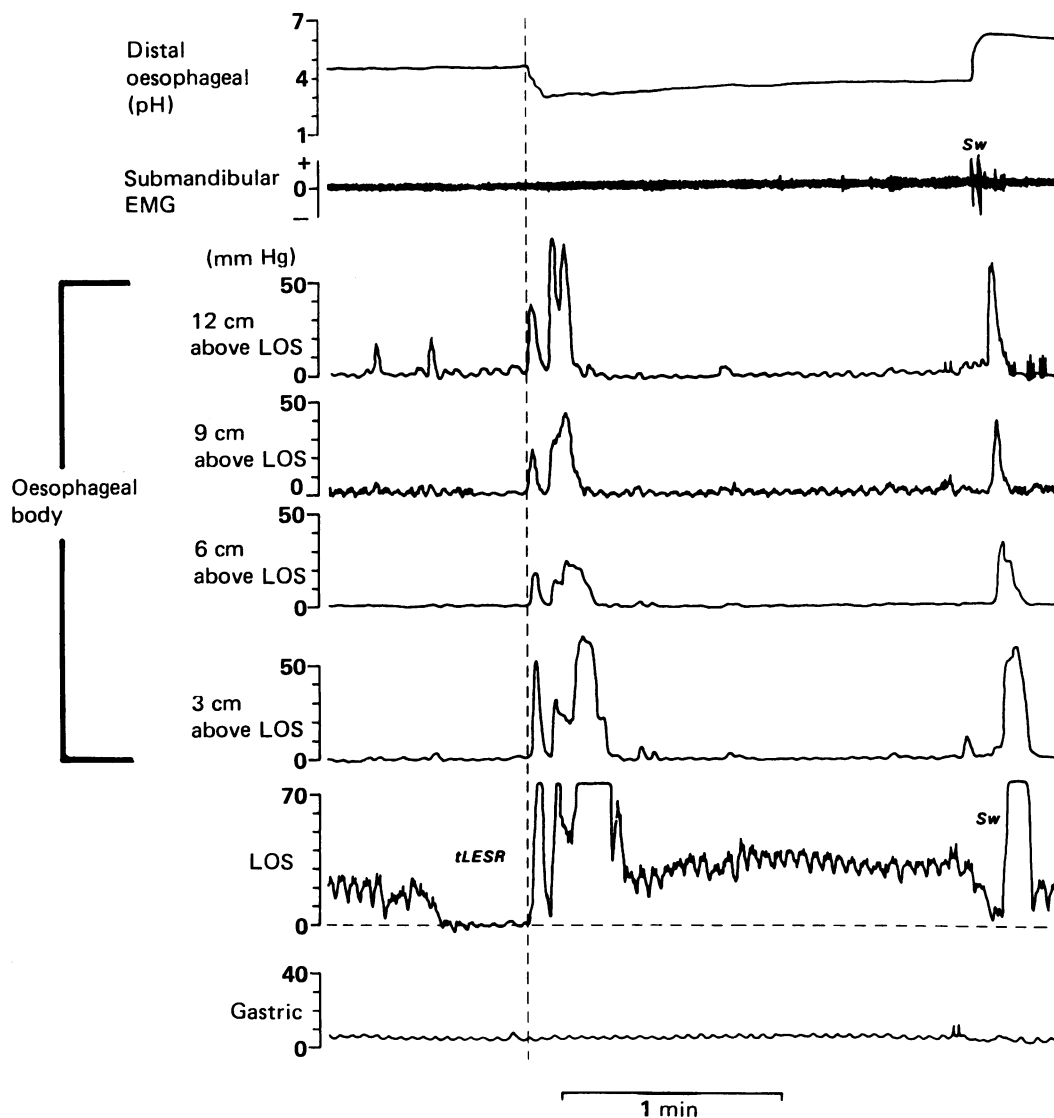


Figure 3: Example of a transient lower oesophageal sphincter relaxation associated with gastro-oesophageal acid reflux recorded in an asymptomatic smoker. Lower oesophageal sphincter pressure is referenced to gastric pressure with the horizontal dotted line (0 mmHg) representing mean intragastric pressure. Note that although the transient lower oesophageal sphincter relaxation persisted for almost 30 seconds, acid reflux did not occur until just prior to lower oesophageal sphincter contraction. In many other instances, acid reflux did not occur at all. Also note the absence of a submandibular electromyographic signal before, during, or after the transient lower oesophageal sphincter relaxation.

pressure values while the subjects were actually smoking cigarettes could not be reliably determined because of the numerous recording artifacts induced by smoking. Specifically, subjects swallowed more frequently, inhaled deeply, and often coughed. Swallowing frequency during the smoking period averaged 2.1 (0.9) per minute compared to 1.1 (0.9) per minute prior to smoking and 1.2 (0.6) per minute after smoking ($p < 0.01$). The subjects took an average of 22 minutes to complete the task of smoking the three cigarettes. As is evident in Figure 2, even this amount of intensive smoking did not affect resting lower oesophageal sphincter pressure immediately after the cessation of smoking when the pharmacological effect of smoking would be expected to be the greatest. In fact, there is no statistical difference between the lower oesophageal sphincter pressure values in any of the five minute epochs for either group of subjects, nor is there any difference in the lower oesophageal sphincter pressure value between groups for any five minute epoch. The data on the five minute periods immediately before and after smoking for the asymptomatic smokers is shown in

the Table. Even when examined in this expanded time frame, cigarette smoking was not associated with any consistent effect on the lower oesophageal sphincter pressure during this period when the pharmacological effect of smoking would be maximal.¹¹ Data for the one minute epochs of the smokers similarly showed no acute smoking effect.

TRANSIENT LOWER OESOPHAGEAL SPHINCTER RELAXATIONS

The period of smoking was associated with an increased mean hourly rate of transient lower oesophageal sphincter relaxations in both the asymptomatic smokers and in the smokers with reflux disease. Figure 3 is an example of a transient lower oesophageal sphincter relaxation associated with reflux in a smoker with reflux disease. The individual from whom this recording was obtained had one of the higher mean lower oesophageal sphincter pressure values of the group of smokers (12 mmHg) and exhibited acid reflux with two of the five transient lower oesophageal sphincter relaxations recorded during the experiment. As

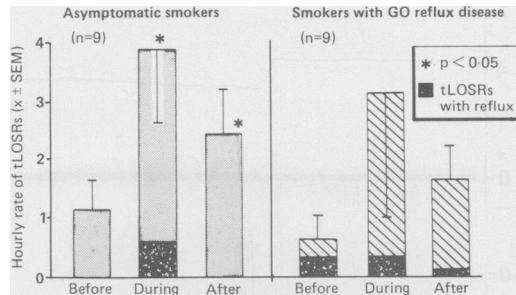


Figure 4: Cumulative data on the rate of occurrence of transient lower oesophageal sphincter relaxations in the asymptomatic smokers (left) and smokers with reflux disease (right). In both groups of subjects, the period of smoking and after smoking were associated with an increased hourly rate of transient lower oesophageal sphincter relaxation. These differences achieved statistical significance only in the case of the asymptomatic smokers predominantly because over half of the patients with reflux disease had lower oesophageal sphincter pressure values too low to meet the criteria for having transient lower oesophageal sphincter relaxations. A relatively small proportion of the transient lower oesophageal sphincter relaxations were associated with acid reflux as indicated by the stippled areas.

illustrated in Figure 4, however, when the data on all subjects were analysed, most transient lower oesophageal sphincter relaxations were not associated with acid reflux detected by the pH electrode. Although the hourly rate of transient lower oesophageal sphincter relaxations increased from a mean value of just over one to a value of almost four in the asymptomatic smokers, only 15% of these were associated with acid reflux. Similar values were obtained in the group of smokers with gastro-oesophageal reflux disease. The increased hourly

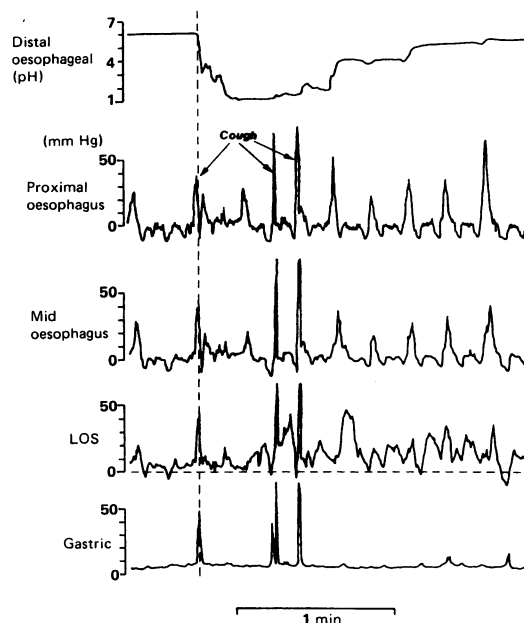


Figure 5: Gastro-oesophageal acid reflux event occurring in a smoker with reflux disease during the smoking period. Lower oesophageal sphincter pressure is referenced to gastric pressure with the horizontal dotted line (0 mmHg) representing mean intragastric pressure. Coughing (arrows) was associated with abrupt increases in intra-abdominal (bottom tracing) and intrathoracic pressure. As was typical of manometric records obtained during smoking, there were wide intrathoracic and lower oesophageal sphincter pressure fluctuations with somewhat laboured respiration and the swallow frequency was often three to four per minute, considerably above normal. The lower oesophageal sphincter pressure value immediately prior to reflux was 5 mmHg and was apparently overcome by the abdominal strain associated with coughing resulting in acid reflux.

rate of transient lower oesophageal sphincter relaxations in the smokers with reflux disease did not achieve statistical significance primarily because of the large SEM in values observed in this group. This is partly explainable by the fact that resting lower oesophageal sphincter pressure was less than 5 in several individuals of this group for a significant proportion of the recording period and thus, they could rarely meet the criteria of definition for transient lower oesophageal sphincter relaxations. The non-smoking controls had a mean of 2.4 transient lower oesophageal sphincter relaxations per hour, 10% of which were associated with acid reflux; comparable figures to those obtained from the asymptomatic smokers.

GASTRO-OESOPHAGEAL ACID REFLUX

Although transient lower oesophageal sphincter relaxations were not often associated with acid reflux, acid reflux did occur. In many instances reflux was prompted by coughing as illustrated in Figure 5 or deep inspiration as illustrated in Figure 6. Such instances invariably occurred during periods of low lower oesophageal sphincter pressure; about 5 mmHg in each of the cases illustrated. Note that there is no decrease in lower oesophageal sphincter pressure before the reflux event suggestive of a transient lower oesophageal sphincter relaxation. The profile of mechanisms by which reflux occurred was similar in both the asymptomatic smokers and in the smokers with oesophagitis so the reflux data on the two groups were combined and illustrated in Figure 7. The number of reflux events per hour increased from a baseline value of 0.6 to a value of 2.8 during the period of smoking. Although the increased rate of reflux reflected increases in events attributable to all mechanisms, the majority of the increase during the smoking period and immediately afterward was attributable to the mechanisms of deep inspiration and coughing. Of particular note, the fraction of reflux events attributable to transient lower oesophageal sphincter relaxations increased only slightly during the smoking period and returned to its baseline value in the post smoking period. Data from the non-smokers were comparable with that of the smokers in terms of the number of reflux events (0.4 per hour) but dissimilar in terms of reflux mechanism. One hundred per cent of reflux events in the non-smokers were attributable to transient lower oesophageal sphincter relaxations while none were attributable to mechanisms associated with low lower oesophageal sphincter pressure.

Discussion

The aim of this study was to investigate whether or not cigarette smoking promoted gastro-oesophageal acid reflux and, if so, by what mechanism. The major findings were that: (1) the lower oesophageal sphincter pressures of smokers, regardless of the presence or absence of symptomatic gastro-oesophageal reflux disease, were significantly lower as a group than that of non-smokers and (2) the period of smoking was associated with an increased rate of acid reflux events but these reflux events occurred predominantly by stress induced mechanisms such as deep inspiration or coughing, mechanisms that would be expected to be operative only

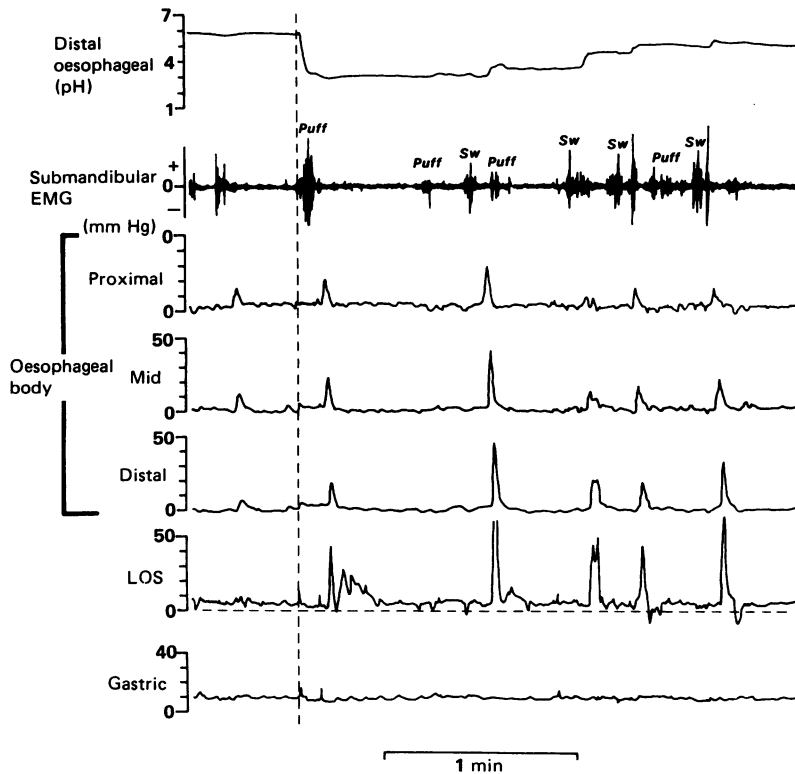


Figure 6: Manometric tracing showing a gastro-oesophageal acid reflux event occurring during smoking in a subject with reflux disease associated with inspiration. Lower oesophageal sphincter pressure is referenced to gastric pressure with the horizontal dotted line (0 mmHg) representing mean intragastric pressure. The vertical dotted line, indicating the moment of reflux is associated with a slight increase in intra-abdominal pressure, a lower oesophageal sphincter pressure of 4 mmHg, and a submental electromyographic signal associated with puffing on a cigarette. Because of the extremely low resting lower oesophageal sphincter pressure, even the slight increase in intra-abdominal pressure associated with the puff on a cigarette overcame the sphincter, resulting in acid reflux.

during periods of reduced lower oesophageal sphincter pressure.

The finding that cigarette smoking does not acutely effect lower oesophageal sphincter pressure is contrary to previous published work. Dennish *et al* and Stanciu *et al* reported an acute reduction in lower oesophageal sphincter pressure as an immediate consequence of cigarette smoking.¹⁴ The comparable period in our study would be the first five minutes after the completion of the smoking task, and, as clearly evident in Figure 2 and the Table, no such reduction was observed. The basal lower oesophageal sphincter pressure of almost all of the smokers was chronically low, however, and conceivably this was a long lasting effect of smoking. Our smokers with reflux disease were older than the asymptomatic smokers and had slightly lower lower oesophageal sphincter pressures as a group. The asymptomatic smokers were of similar ages to the non-smokers, however, and had significantly lower lower oesophageal sphincter pressures suggesting this to be a smoking related effect rather than an age effect. The time course of this putative effect on lower oesophageal sphincter pressure and the potential for recovery will need to be evaluated in another investigation. Such a chronic effect on lower oesophageal sphincter function may be partly explained by the pharmacokinetics of nicotine. Normal smokers have blood nicotine concentrations subject to circadian variation characterised by high levels during the day and progressively lower levels during the night. Even eight hours after smoking, however, persistent blood nicotine concentrations were present implying that the drug

effect can persist for at least that long.^{11,12} Nicotine has been shown to reduce the lower oesophageal sphincter pressure of opossums in a dose dependent fashion,¹³ but the doses tested (5–60 µg/kg) are difficult to equate to those attained by people smoking cigarettes (16–50 ng/ml).¹¹ We did not do the experiment that would be necessary to determine whether or not smoking has a short term effect on the lower oesophageal sphincter pressure of an individual who had never smoked cigarettes.

The data on transient lower oesophageal sphincter relaxations were surprising. Not only were a minority of reflux events attributable to transient lower oesophageal sphincter relaxations, but most transient lower oesophageal sphincter relaxations were not associated with acid reflux detected by the pH electrode. Although the data illustrated in Figure 4 relate only to the occurrence of reflux events resulting in a fall of oesophageal pH to a value of less than 4, analysing the data for any detectable fall in oesophageal pH did not significantly alter the findings. The increased occurrence of transient lower oesophageal sphincter relaxations during smoking suggests that they are serving a function directly accentuated by smoking. Previous work suggests that transient lower oesophageal sphincter relaxations allow for gas venting from the stomach.^{14–16} Smoking might be expected to be associated with a significant amount of air swallowing and the resultant gastric distension may serve as the stimulus of triggering transient lower oesophageal sphincter relaxations.¹⁷ Although there is a significant body of data suggesting that patients with reflux disease have an increased number of transient lower oesophageal sphincter relaxations accounting for roughly two thirds of their reflux events, those patients were studied while at rest.^{5–7} On the other hand, the present study introduced a potential stimulant for reflux, smoking, and in this

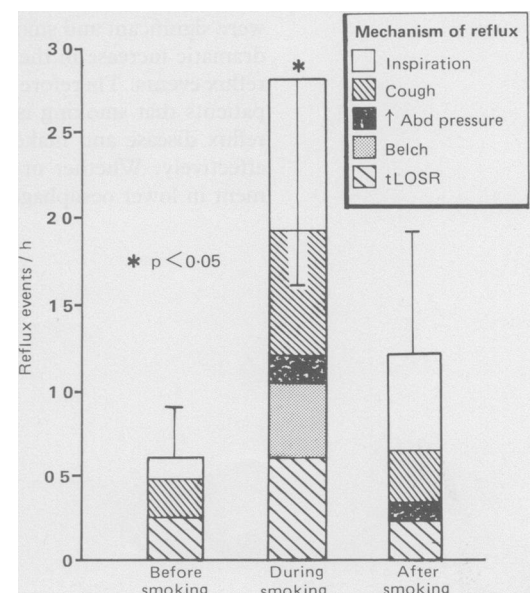


Figure 7: Summary data on the mechanism of gastro-oesophageal acid reflux. Data from the asymptomatic smokers and smokers with reflux disease were grouped because the mechanisms observed in each group were similar to each other. The period of smoking was accompanied by a significant increase in the rate at which reflux events occurred. More than half of reflux events in each condition occurred with coughing or deep inspiration; a minority were associated with transient lower oesophageal sphincter relaxations. The relative proportion of reflux events attributable to coughing, inspiration, and straining increased as a result of smoking.

condition transient lower oesophageal sphincter relaxations would not seem to be the dominant mechanism of reflux.

The period of smoking was associated with an increased incidence of gastro-oesophageal acid reflux. The mechanisms by which this occurred were predominantly of deep inspiration and coughing, both activities stimulated by the act of smoking. This raises the question of what came first, the diminished lower oesophageal sphincter pressure that leaves individuals susceptible to mechanisms of stress reflux or oesophagitis which may be a consequence of the reduced lower oesophageal sphincter pressure and also cause further reduction of lower oesophageal sphincter pressure.¹⁸ In this regard, the data on asymptomatic smokers are particularly interesting because they score intermediately between groups of non-smokers and patients with oesophagitis suggesting that chronic smoking may set in motion the cycle of increased reflux leading to further reduction of lower oesophageal sphincter pressure leading to more reflux. Ultimately this cycle could result in the development of peptic oesophagitis. In any event, the asymptomatic smokers studied were unlike previous groups of control subjects studied; their lower oesophageal sphincter pressures were lower and they refluxed by mechanisms not previously encountered in normals. In a major analysis of the mechanism of gastro-oesophageal acid reflux, Dent *et al* showed that 98% of reflux events in normal volunteers were caused by transient lower oesophageal sphincter relaxations, a mechanism that accounted for less than 20% of reflux events in asymptomatic smokers during periods of smoking.

In summary, smoking does seem to impact significantly on gastro-oesophageal reflux disease. Although acute effects on lower oesophageal sphincter pressure were not seen, pre-existing differences in lower oesophageal sphincter pressure were significant and smoking was associated with a dramatic increase in the rate of occurrence of acid reflux events. Therefore it seems justified to advise patients that smoking is likely to exacerbate their reflux disease and make it more difficult to treat effectively. Whether or not the observed impairment in lower oesophageal sphincter function was

directly attributable to chronic effects of smoking and whether or not these would show recovery over time if individuals ceased to smoke remains to be determined.

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