

Heartburn of Pregnancy

"A warm discomfort situated in the epigastrium or retrosternal region, usually radiating up to the throat or more rarely across the chest, and . . . usually associated with intake of food or change in posture."¹ This is a common symptom and one that most people experience from time to time and come to recognize as a benign nuisance. In pregnancy it is particularly common and troublesome, occurring in two thirds of Caucasian woman in Sheffield and Liverpool and in a similar proportion of Negro women in Chicago.² It occurs in particular during the second and third trimesters of pregnancy. A previous suggestion³ that it is relieved during the last four weeks of pregnancy, when the fetal head descends into the pelvis, has not been substantiated.² This suggests that raised intra-abdominal pressure is not the main cause of heartburn, and recent research indicates that more subtle mechanisms are at play.

The lower oesophageal sphincter maintains the barrier between the stomach and the oesophagus. The pressure that it exerts can be measured by traversing this area with an open-ended tube filled with fluid which is constantly infused during the measurement. By this procedure various artefacts have been eliminated, and a true and reproducible recording can be obtained. By this technique it has been shown that, so long as this sphincter is working and gastric contents do not enter the lower oesophagus, patients do not have symptoms of reflux oesophagitis, even if they have a hiatus hernia. The functioning of this sphincter appears to be of more importance than whether the stomach is above or below the diaphragm.^{4,5} The integrity of the sphincter is reduced by smoking⁶ and a fall in the blood level of gastrin.⁷

If gastrin can do this why not other hormones? In relation to heartburn of pregnancy this would seem to be a useful line of study, for the hormonal changes that occur during pregnancy are known to affect the functioning of smooth muscle in other parts of the body, such as the ureters. In a recent study the pyloric sphincter has been shown to be incompetent in patients with pregnancy heartburn, which would be in keeping with the idea that hormonal factors may be affecting the functioning of smooth muscle in various organs.

Once the lower oesophageal sphincter is incompetent, gastric contents enter the lower oesophagus. Acid in this area produces the pain, and heartburn is also caused by reflux of bile through pyloric and lower oesophageal sphincters.^{8,9} Perhaps reflux of bile into the oesophagus is more important in the pathogenesis of heartburn than the reflux of gastric acid.¹⁰

The histological consequences of gastro-oesophageal reflux have been accurately assessed in a careful study. Suction biopsy specimens were obtained from patients with and without reflux.¹¹ The earliest changes in the lower oesophageal mucosa were basal cell hyperplasia of the squamous epithelium and location of the papillae close to the epithelial surfaces. These changes are the ones that would be expected if there was an increased turnover of epithelial cells in response to the oesophageal insult. Eighty-five per cent. of subjects with heartburn have been shown to have these early histological changes in the lower oesophageal mucosa, whereas these changes were not present in 90% of normal controls.¹¹ An interesting point from this study was that seven of the patients with heartburn who had histo-

logical changes did not have demonstrable gastro-oesophageal reflux. It is suggested that in these patients reflux was intermittent, which is why it was not detected at the time of the investigation. There were also nine patients in this study who had reflux but who had no symptoms. About half of these patients had histological changes. Thus there are some patients who have asymptomatic reflux associated with histological changes in the lower oesophageal mucosa.

Most patients who have occasional mild heartburn learn to avoid conditions that provoke the symptoms. Frequent small meals, milk, alkali, and avoidance of bending or lying flat frequently improve the symptoms. Obese patients should be advised to lose weight, and it is surprising how often the symptoms then improve. There is recent evidence that metoclopropamide 10 mg three times a day is more effective than a placebo in relieving heartburn,¹² and it can be tried in resistant cases. Unless the symptoms are very severe it would not seem justifiable to use it during pregnancy. Antacid preparations that float on the surface of the gastric contents and are said to prevent reflux by blockage of the cardiac opening have not been proved to be better than simple antacids, but they are worth a trial in resistant cases.

- 1 Tuttle, S. G., Rufin, F., and Bettarello, A., *Annals of Internal Medicine*, 1961, 55, 292.
- 2 Atlay, R. D., Gillison, E. W., and Horton, A. L., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1973, 80, 63.
- 3 Rodway, H. E., and Shelley, U., *Journal of Obstetrics and Gynaecology, of the British Commonwealth*, 1935, 42, 107.
- 4 Winans, C. S., and Harris, L. D., *Gastroenterology*, 1967, 52, 773.
- 5 Cohen, S., and Harris, L. D., *New England Journal of Medicine*, 1971, 284, 1053.
- 6 Stanciu, C., and Bennett, J. R., *Gut*, 1972, 13, 318.
- 7 Castell, D. O., and Harris, L. D., *New England Journal of Medicine*, 1970, 282, 886.
- 8 Bernstein, L. M., and Baker, L. A., *Gastroenterology*, 1958, 34, 760.
- 9 Gillison, E. W., Capper, W. M., Airth, G. R., Gibson, M. J., and Bradford, I., *Gut*, 1969, 10, 609.
- 10 Gillison, E. W., Nyhus, L. M., and Duthie, H. L., *British Journal of Surgery*, 1971, 58, 864.
- 11 Ismail-Beigi, F., Horton, P. F., and Pope, C. E., *Gastroenterology*, 1970, 58, 163.
- 12 Johnson, A. G., *British Medical Journal*, 1971, 2, 25.

Malignancy of Bronchial Adenoma

The bronchial adenoma is a white, somewhat circumscribed tumour arising from the wall of a bronchus. It is usually central, deriving from one of the major bronchi, and it leads to collapse of the distal lung, with inevitable superadded infection. The main symptoms are cough, haemoptysis, wheezing, and fever. The rarer peripheral tumour is usually discovered during a routine radiological examination of the chest. The mass that projects into the bronchial lumen is only a small part of a much more extensive tumour that spreads outside the confines of the bronchus. Bronchial adenomata form about 1% of all primary lung tumours and are traditionally described as slow-growing. But their malignant potentiality is well recognized, for they infiltrate locally and may metastasize to distant organs.¹⁻⁵

Histologically three main types are recognized. The commonest is the carcinoid tumour, which is similar in structure to the better known argentaffinoma of the gastro-intestinal tract. It arises from the cells of Kulshitzky of the bronchial mucosa and from neurosecretory cells of mucous glands. It has recently been noted that similar neurosecretory granules may be found in the oat-cell

carcinoma, and it would appear that this tumour is a highly malignant variant of the bronchial carcinoid.⁶ Less common are the adenoid cystic carcinoma and the mucoepidermoid carcinoma, tumours noted most often in the salivary glands. The adenoid cystic carcinoma, also called the cylindroma, consists of trabeculae, columns, and cords of epithelial cells, some enclosing cystic spaces, which are surrounded by a dense, hyaline stroma. The mucoepidermoid carcinoma contains a mixture of squamous-cell and mucus-secreting glandular elements. A true mucus-secreting adenoma has also been described, but it is very rare.⁷

Recently A. D. Turnbull and his colleagues have reviewed 61 cases of bronchial adenoma which had occurred over a period of 43 years.⁸ These comprised 44 carcinoid tumours, 12 mucoepidermoid carcinomata, and 5 adenoid cystic carcinomata. Most of these tumours occurred in patients between the ages of 40 and 70 years, and while the sex incidence was equal in the carcinoid group there was a male predominance in the other two groups of tumours. None of the cases of carcinoid tumour showed the typical endocrine syndrome. The most conspicuous finding in this series was the high degree of malignancy of the tumours. Only 59% of the patients with carcinoid tumour and 60% of those with adenoid cystic carcinoma survived for five years, while all those with mucoepidermoid carcinoma had died during that period of time. This is especially surprising, as mucoepidermoid carcinoma is usually regarded as the most benign type of bronchial adenoma,⁷ other than the rare mucus-secreting adenoma, which was not encountered in this series.

The observations of Turnbull and his colleagues once again contradict the traditional teaching that the various types of bronchial adenoma behave in a benign fashion and are usually compatible with prolonged survival. The time has surely come to expunge the term bronchial adenoma, and to group the tumours that have been included under this heading as bronchial carcinoids, mucoepidermoid carcinomata, and adenoid cystic carcinomata. While they are certainly less malignant than the usual varieties of lung cancer—the oat-cell carcinoma, adenocarcinoma, and squamous-cell carcinoma—their serious nature must be fully acknowledged.

¹ Zellos, S., *Thorax*, 1962, 17, 61.

² Wilkins, E. W., Darling, R. C., Soutter, L., and Sniffen, R. C., *Journal of Thoracic and Cardiovascular Surgery*, 1963, 46, 279.

³ Batson, J. F., Gale, J. W., and Hickey, R. C., *Archives of Surgery*, 1966, 92, 623.

⁴ Verska, J. J., and Connolly, J. E., *Journal of Thoracic and Cardiovascular Surgery*, 1968, 55, 411.

⁵ O'Grady, W. P., McDivitt, R. W., Holman, C. W., and Moore, S. W., *Archives of Surgery* 1970, 101, 558.

⁶ Bensch, K. G., Corrin, B., Pariente, R., and Spencer, H., *Cancer*, 1968, 22, 1163.

⁷ Donahue, J. K., Weichert, R. F., and Ochsner, J. L., *Annals of Surgery*, 1968, 167, 873.

⁸ Turnbull A. D., Huvos, A. G., Goodner, J. T., and Beattie, E. J., *Annals of Thoracic Surgery*, 1972, 14, 453.

C. C. Addison of the use of liquid tin in glassmaking and of liquid sodium as the cooling liquid in fast nuclear reactors; a model showing the factors responsible for explosions inside oiltankers' fuel compartments; and several applications of linear motors.

Of more direct interest to doctors was a comparison of the visual systems of the cat and man, shown by a team from the Physiological Laboratory at Cambridge. Studies on the cat using sinusoidal gratings had shown that single neurons in the visual cortex were responsive over only a narrow range of spatial frequencies and that the orientation of the grating was also critical. It seems that the human visual cortex contains neurons with similar specifications, and both fatigue and adaptation of these receptors can be shown in simple psychological tests. Doctors at St. George's Hospital, London, showed their technique for measuring the muscular tone in the walls of veins on the back of the hand. Changes in this tone are relatively easy to measure and correlate well with the clinical state of the patient after a coronary thrombosis. The technique is also useful in assessing local response to infused drugs. A popular and elegant demonstration was one from the Physiology Laboratory at Oxford, in which position sense at the elbow joint was deceived by the application of an electrical vibrator to the muscles of the upper arm. This showed the role of muscle stretch receptors in providing sensory information about angulation at the adjacent joints.

Among all the 26 exhibits, however, there seemed little doubt of the one most likely to appeal to every visitor: this was an ingenious development from the National Physical Laboratory, Teddington of a slide projector which switched on and off, moved the slides forward and back, and focussed them—all in response to spoken commands. The speech is analysed by a device which extracts from the sounds features common to all speakers, namely vowel quality, fricative quality, and gaps of silence.

Lanolin Allergy

Allergic contact dermatitis is a well-recognized hazard in industry, with cosmetic applications, and topically applied medicaments such as analgesic or antibiotic compounds. But it is still insufficiently appreciated that widely used skin preparations containing lanolin may cause chronic, troublesome, and puzzling eczematous dermatitis, often attributed wrongly to "nervous" factors, thus frustrating an otherwise simple therapeutic task.

While contact sensitivity due to lanolin had been reported as long ago as 1930,¹ its frequency had largely escaped detection until recent years because of the diagnostic pitfalls and limitations of patch testing, which is still the principal and in all but a few research centres the only method of diagnosing allergic contact dermatitis. Dermatologists with specialized experience in this field²⁻⁴ drew attention to the fact that, while lanolin is neither a very potent nor a very common sensitizer, false-negative patch tests are frequent in lanolin-sensitive patients. N. Hjorth and C. Trolle-Larsen³ suggested that 30% wool alcohols in a mixture of olive oil and petroleum jelly should be used when patch-testing for suspected lanolin sensitivity, having found an incidence of 30% of false-negative patch tests when using a mixture of 5% salicylic acid and lanolin,

Science on Show

A close relationship between science and industry has been part of the British tradition since the times of Sir Humphrey Davy, and this was well illustrated at the Royal Society Conversazione held last week. The exhibits concerned with the physical sciences included a glass-reinforced cement developed by Pilkingtons; a demonstration by Professor