Models of gastric emptying

D. F. STUBBS¹

From the Department of Physiology, Guy's Hospital Medical School, London

SUMMARY Some empirical and theoretical models of the emptying behaviour of the stomach are presented. The laws of Laplace, Hooke, and Poisseuille are used to derive a new model of gastric emptying. Published data on humans are used to test the model and evaluate empirical constants. It is shown that for meals with an initial volume of ≥ 300 ml, the reciprocal of the cube root of the volume of meal remaining is proportional to the time the meal is in the stomach. For meals of initial volume of < 300 ml the equation has to be corrected for the fact that the 'resting volume' of gastric contents is about 28 ml. The more exact formula is given in the text. As this model invokes no neural or hormonal factors, it is suggested that the gastric emptying response to the volume of a meal does not depend on these factors. The gastric emptying response to the composition of the meal does depend on such factors and a recent model of this process is used to evaluate an empirical constant.

Many authors have proposed equations describing the emptying of a meal from the stomach with time. If V is the volume of a meal in the stomach at a given time and t is the time since the meal was given, then the differential dV/dt describes the rate of gastric emptying. Table 1 gives various empirically justified relationships of dV/dt to V. They belong to a family of equations of the form:

¹Present address: Anti-Inflammatory Disease Products, The Upjohn Company, Kalamazoo, Michigan 49001, USA. Received for publication 26 September 1976.

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -\mathrm{c}V^{\mathrm{p}}$$

where p is a constant and c may or may not be a constant for the particular meal employed. As the quoted equations have varying degrees of theoretical, empirical, and practical value, it was felt that a further attempt at modelling gastric emptying was needed.

The present paper is concerned with evaluating the constants of the newly proposed model, given in

Table 1 Some equations of gastric emptying of form $\frac{dV}{dt} = -c V^p$ where V = volume of meal in stomach,

t =	time,	р	is c	i consta	nt, a	nd c	may c	or may	not i	be	constant
-----	-------	---	------	----------	-------	------	-------	--------	-------	----	----------

ρ	c	Subjects	Source
0.00	Constant independent of V	Human neonates	Husband and Husband (1969)
	· · · · · · · · · · · · · · · · · · ·	Human adults	Moberg and Carlberger (1973)
0.50	Constant independent of V	Human adults	Hopkins (1966a, b)
	•	Human adults	George (1968)
1.00	Constant independent of V	Codfish	Tyler (1970)
	-	Rats	Reynell and Spray (1956)
		Dogs	Weisbrodt et al. (1969)
		Human adults	Salamanca (1943)
		Human adults	Hunt (1949)
		Human adults	Griffiith et al. (1968)
		Human adults	Brömster (1969)
		Human adults	Harvey et al. (1970)
		Human adults	Van Dam (1972)
1.33	Constant × $\left(1 - \left(\frac{\text{constant}}{V}\right)\right)$	Human adults	Present paper
2.00	Constant $\times \left(1 - \frac{\text{constant}}{V}\right)^2$	Dogs	Tamarit (1955)

Models of gastric emptying

the Table. The theoretical basis for the new model is given in an appendix.

We have as cur present equation describing gastric emptying:

where C is a constant related to the composition of the meal, but not the volume; p and n are constants; and v is the volume of the meal and/or secretions in a 'resting' stomach. Integrating between limits V_t at time = t and V_0 at time = 0 we have:

$$-Ct = V_t^{1-p}F(V_t) - V_0^{1-p}F(V_0)....(2)$$

where $F(V) = \left(\frac{-1}{n}\right) \sum \frac{x^i}{y+i}$ (2a)

where
$$\mathbf{x} = (\mathbf{v}/\mathbf{V})^n$$
 (2b)

and
$$y = (1-p)/(-n)$$
 (2c)

and $0 \le i \le \infty$ in integral steps.

If we put $t = t_{0.5}$ at $V_t = 0.5 V_0$ we have from eqn. (2):

$$-C = \frac{V_0^{1-p}}{t_{0.5}} \left[0.5^{1-p} F(0.5V_0) - F(V_0) \right] \dots (3)$$

Thus putting (3) into (1) and re-arranging, we have:

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \frac{V_0^{1-p}}{t_{0.5}} \left[0.5^{1-p} F(0.5V_0) - F(V_0) \right] V^p \times \left[1 - (v/V)^n \right]$$
(4)

At time t = 0 we have:

where $F^{*}(V_{0}) = [0.5^{1-p}F(0.5V_{0}) - F(V_{0})] \times [1 - (v/V_{0})^{n}].....(5a)$

Putting (3) into (2) and re-arranging we have:

$$V_{t} = (F(V_{t}))^{-1/(1-p)} V_{0}[F(V_{0}) + \frac{t}{t_{0.5}} \times (0.5^{1-p}F(0.5V_{0}) - F(V_{0}))]^{1/(1-p)}.$$
 (6)

We now consider the case when V becomes so large that $(v/V)^n$ approximates to zero.

By similar reasoning to that above we obtain the analogous large-meal equations:

$$-Ct = V_t^{1-p} \left(\frac{1}{1-p}\right) - V_0^{1-p} \left(\frac{1}{1-p}\right) (2')$$
$$-C = \frac{V_0^{1-p}}{t_{0.5}} \left[0.5^{1-p} \left(\frac{1}{1-p}\right) - \left(\frac{1}{1-p}\right)\right]$$
....(3')

203

$$\frac{dV}{dt} = \frac{V_0^{1-p}}{t_{0.5}} \frac{(0.5^{1-p}-1)}{(1-p)} V^p \quad \dots \dots \quad (4')$$

$$V_t = V_0 \left(1 + \frac{t(0 \cdot 5^{1-p} - 1)}{t_{0.5}(1-p)} \right)^{1/(1-p)} \dots (6')$$

From the above we deduce what can also be deduced directly—that is, as V tends to infinity:

$$F(V) \rightarrow \left(-\frac{1}{n} \right) / (1-p)$$
 (7)

and
$$F^{*}(V) \to 'F^{*}(V) = \frac{0 \cdot 5^{1-p} - 1}{(-n)(1-p)}$$
 (8)

Methods and results

We wish to determine the constants p, n, and v in equation (1). The nature of the equation with its non-explicit solution forces us to use an indirect approach.

DETERMINATION OF p

Data were taken from Hunt (1949) where a test meal of 750 ml was given to 21 normal adult male subjects. In all 183 test meals were given. It was assumed that the value of $(v/V)^n$ was sufficiently small to use the analogous large-meal equations. From Hunt's mean curve the differential dV/dt could be approximated over a five minute interval. As values up to 110 minutes were available, 23 different points were obtained. The gastric secretion added over each five minute interval was corrected for. A computer programme which minimised the squared residuals was used. Fitting equation (1') it was found that p = 1.322. Fitting equation (2') it was found that p = 1.338. In neither case was the possible range of p calculable from this particular grogramme. The conclusion drawn is that p = 4/3.

DETERMINATION OF n

Again using data from Hunt (1949) and a computer programme which minimised the squared residuals, an attempt was made to fit equation (1). The equation was resistant to the iterative procedure used but generated the following values: p = 1.33, n = 0.50, and $10 \le v \le 50$ ml. As the value of p was the same as before and the value of n was constant for various attempts, it was taken that n = 1/2.

DETERMINATION OF V

Hunt and Stubbs (1975) have shown that for meals where $V_0 \ge 300$ ml the half-time, 't_{0.5}, can be given by:

$$V_{t_{0.5}} = V_0(0.1797 - 0.1670e^{-K}) \dots (9)$$

where K is the caloric density (Kcal/ml) of the meal. For meals where $V_0 < 300$ ml, eqn. (9) predicts the half-time, 't_{0.5}, with increasing error as V_0 is reduced. Hunt and Stubbs (1975) assumed an equation of type (1') for their work. The error of prediction is now accounted for and utilised to evaluate v. If eqn (5') is divided by eqn (5) we have (assuming observed and predicted are the same):

Using p = 1.33 and n = 0.5 values of z may be found using eqns (5a) and (8) and computer generation. Thus a table of z and x (eqn 2b) may be drawn up.

Data for small volume test meals were taken from the literature (Table 2). Using Table 2 and eqn (9) it was possible to calculate the ratio $t_{0.5}/t_{0.5}$ (\equiv z, eqn 10). Using a z-x table it was possible to find the corresponding value of $x = (v/V_0)^{1/2}$. Thus v could be computed. It was found that v = 28.45 ml (\pm SD 28.84; SEM \pm 6.41).

DETERMINATION OF ALL CONSTANTS

The above data, methods, and results suffer from the disadvantages that they are derived from pooled data and they give little guide to inter-individual differences. These problems can be partially resolved in the following manner. Raw data (values and times) can be fitted to the differential equation (1) by a computer programme which minimises squared residuals. The programme estimates the four unknown parameters with poor precision for the following reasons: (1) the fitting of raw data to a differential equation with four parameters is a procedure at the limits of power of the programme and the standard deviations of the estimated parameters is very large; (2) the number of test meals for any one subject and meal type is small; (3) the coefficient of variation of the test meal method is not small. The present data showed that for any subject given the same meal with the same recovery time on more than one occasion than the standard deviation of the mean volume recovered. This is noticeable with any test meal data set since when a smooth curve is drawn through the data a wide spread occurs.

Given the above problems, this procedure was used on each subject of Hunt (1949). Because of the small number of meals per subject, it was not possible to correct for gastric secretions as was done for the pooled data. Thus the programme was run using either the total recovered volume (VT) or the volume of meal remaining (VMR), where secretions are subtracted. The true values are probably intermediate between the ones obtained. The mean values obtained for the parameter p were (using VT) 1.27 (SEM ± 0.072) and (using VMR) 1.33 (SEM \pm 0.078). In neither case was the value significantly different from 1.25 or 1.33 but the values were significantly different from 1.0 and 1.5 (P < 0.01). The mean values obtained for the parameter n were (using VT) 0.47 (SEM \pm 0.050) and (using VMR) 0.41 (SEM \pm 0.056). In neither case was the value significantly different from 0.5, but it was significantly different from 0.33 (P < 0.05), in the case of VT only. The mean values obtained for the parameter v were (using VT) 25.10 (SEM \pm 9.26) and (using

Predicted half-life (min) **Observed** half-time Ratio: K. caloric density Source V_o Initial Volume t 0.5 (min) to.s/'to.s (Kcal/ml) (ml) $t_{0.5} = V_0(0.1797 - 0.1670e^{-K})$ 4.94 1.58 7.8 0.36 25 0.36 3.16 8.0 2.53 2 50 0.36 6.32 9.0 1.42 3 100 14.2 1.12 0.36 12.64 4 5 200 6.0 3.14 1.91 0.00 150 7.5 2.95 2.54 6 200 0.00 5.92 16.0 2.70 1.00 7 50 11.83 25.0 2.11 8 100 1.00 35.48 43.0 1.21 9 300 1.00 9.0 0.87 10.36 10 300 0.14 22.60 23.0 1.02 11 300 0.47 34.0 1.01 0.90 33.54 300 12 43.0 1.11 38.82 13 300 1.20 46.0 1.30 35.48 14 300 1.00 36.0 0.89 40.26 15 300 1.30 11.39 17.0 1.49 0.14 16 330 56.0 0.98 57.03 350 2.30 17

Table 2 Half-times, as observed and predicted, for gastric emptying of meals of small volume and variable composition

Sources: meals 1-6: Erskine and Hunt (1975); meals 7-9: Hunt and Fisher (1975); meals 10-13: Moberg and Carlberger (1974); meal 14: Davies et al. (1971); meal 15: Brömster (1969); meal 16: Hunt and MacDonald (1954); meal 17: Harvey et al. (1970).

VMR) 38.74 (SEM \pm 9.29). The large standard error of the mean signifies a large inter-individual variation for the parameter v, unlike the case for the parameters p and n which are similar between individuals.

A second set of data was provided by Hunt and Fisher (unpublished). They gave eight kinds of test meals to 13 subjects. The initial volume varied from 0.17 to 2.0 kcal/ml. The data were examined in the same way as the approach previously described. The volume of meal remaining (VMR) was the variable examined. The following mean values were obtained: p = 1.33 (SEM ± 0.057), n = 0.46 (SEM ± 0.057), and v = 27.67 (SEM ± 1.72). These parameters did not vary significantly as a function of the volume or composition of the meal.

Discussion

An equation of type (1) will correctly predict the half-time of a small meal. With meals of initial volume greater than or equal to 300 ml an equation of type (1') is adequate. It was found that the constant p = 4/3. In the literature (Table 1) we find $0 \le p \le 2$. In the appendix it is predicted that $1.0 \le p \le 1.33$. It was found that the constant n = 0.5. In the appendix it was predicted that $0.33 \le n \le 0.5$. Further, it was found that the volume of the contents of a 'resting' stomach was about 28 ml. This agrees with the direct empirical value of 22.0 ml (SD \pm 6.5) as found by Williams and Hunt (1973) in healthy adult males.

The given equation of gastric emptying is difficult to apply without computer assistance. For test meals of initial volume greater than or equal to 300 ml the following equation appears to fit the data better than others:

$$V_t^{-1/3} = V_0^{-1/3} - ct$$

The value of equation (1) is that it seems to fit the gastric emptying of meals over all time periods and it predicts that gastric emptying will cease at a finite time and non-zero gastric volume.

The premises of the present model would imply that the gastric response to the volume of a meal is determined by the physical characteristics of the gastric wall and some local hydraulic considerations. No neural or hormonal factors were invoked. Thus the stomach responds to the volume of a meal in a passive fashion. The gastric response to the composition of the meal has been modelled by Hunt and Stubbs (1975) where they implicitly invoked the neural and hormonal factors released by duodenal receptor stimulation. In the present model it was hypothesised that the neural and hormonal factors influencing the gastric response to the composition of a meal act upon the Young's modulus of the gastric wall.

The author wishes to thank J. N. Hunt, F. House, G. Elfring, and A. P. Hopkins for their help and advice.

References

- Brody, D. A., and Quigley, J. P. (1948a). Some mechanical factors in the dynamics of the thin walled spherical viscus. *Bulletin of Mathematical Biophysics*, 10, 25-30.
- Brody, D. A., and Quigley, J. P. (1948b). Measurement of gastric tonus in the normal human. *Federation Proceedings*, 7, 13-14.
- Brömster, D. (1969). Gastric Emptying Rate in Man. An Experimental and Clinical Study Using ¹³¹I-HSA. Brömster: Stockholm.
- Davies, W. T., Kirkpatrick, J. R., Owen, G. M., and Shields, R. (1971). Gastric emptying in atrophic gastritis and carcinoma of the stomach. Scandinavian Journal of Gastroenterology, 6, 297-301.
- Erskine, L., and Hunt, J. N. (1975). Paper in preparation.
- Evans, C. L. (1926). The physiology of plain muscle. Physiological Reviews, 6, 358-398.
- Frank, O. (1910). Die Dehnung einer Kugelformigen Blase. Zeitschrift für Biologie, 54, 531-532.
- George, J. D. (1968). New clinical method for measuring the rate of gastric emptying: the double sampling test meal. *Gut*, 9, 237-242.
- Griffith, G. H., Owen, G. M., Campbell, P. M., and Shields, R. (1968). Gastric emptying in health and gastroduodenal disease. *Gastroenterology*, 54, 1-7.
- Harvey, R. F., Mackie, D. B., Brown, N. J. G., Keeling, D. H., and Davies, W. T. (1970). Measurement of gastric emptying time with a gamma camera. *Lancet*, 1, 16-18.
- Hopkins, A. P. (1966a). The pattern of gastric emptying Journal of Physiology, 182, 144-149.
- Hopkins, A. P. (1966b). Relation between pressure and volume in hollow viscera. Gut, 7, 521-524.
- Hunt, J. N. (1949). A Critical Study of some Aspects of Gastric Function in Man. Thesis University of London: London.
- Hunt, J. N., and Fisher, M. (1975). Paper in preparation.
- Hunt, J. N., and MacDonald, I. (1954). The influence of volume on gastric emptying. *Journal of Physiology*, 126, 459-474.
- Hunt, J. N., and Stubbs, D. F. (1975). The volume and energy content of meals as determinants of gastric emptying. *Journal of Physiology*, 245, 209-225.
- Husband, J., and Husband, P. (1969). Gastric emptying of water and glucose solutions in the newborn. Lancet, 2, 409-411.
- Marbaix, O. (1898). Le passage pylorique. Cellule, 14, 249-332.
- Moberg, S., and Carlberger, G. (1973). Gastric emptying after selective proximal vagotomy in relation to the outcome of the insulin test. *Rendiconti di Gastroenterologia*, **5**, 163-167.
- Moberg, S., and Carlberger, G. (1974). The effect on gastric emptying of test meals with various fat and osmolar concentrations. *Scandinavian Journal of Gastroenterology*, 9, 29-32.
- Nelsen, T. S., and Kohatsu, S. (1971). The stomach as a pump. Rendiconti di Gastroenterologia, 3, 65-71.
- Quigley, J. P., and Brody, D. A. (1950). Digestive tract: intralumen pressures: gastrointestinal propulsion, gastric evacuation, pressure-wall tension relationships. In *Medical*

Physics, vol. 2, pp. 280-292. Edited by O. Glasser. Year Book Publishers: Chicago.

- Reynell, P. C. and Spray, G. H. (1956). The simultaneous measurement of absorbtion and transit in the gastrointestinal tract of the rat. *Journal of Physiology*, 131, 452-462.
- Salamanca, De F. E. (1943). La fisiologia gástrica humana segun los datos de mi procedimento de explonación functionál. Revista Clinica Española, 8, 94-104.
- Stillwell, G. K. (1973). The Law of Laplace: some clinical applications. Mayo Clinic Proceedings, 48, 863-869.
- Tamarit Torres, J. (1955). Una neueva ley de evacuación gástrica. Archivos de Medicina Experimental, 18, 307-328.
- Tyler, A. V. (1970). Rates of gastric emptying in young cod. Journal of the Fisheries Research Board of Canada, 27, 1177-1189.
- Van Dam, A. P. M. (1972). Gastric Emptying Utilizing the Gamma Camera. Schippers: Nijimegen.
- Weisbrodt, N. W., Wiley, J. N., Overholt, B. F., and Bass, P. (1969). A relation between gastroduodenal muscle contractions and gastric emptying. Gut, 10, 543-548.
- Williams, R. H. M., and Hunt, J. N. (1973). Amounts of acid and of chloride in the residual gastric contents in healthy persons. *Guy's Hospital Reports*, **122**, 161-167.
- Winton, F. R., and Bayliss, L. E. (1935). Human Physiology, 2nd edn. Churchill: London.

Appendix

A theoretical basis for equation (1) is here derived.

LAW OF LAPLACE

This has been applied to the stomach by Brody and Quigley (1948a,b), Quigley and Brody (1950), and Hopkins (1966a,b) and to other organs (Stillwell, 1973). Although it relates to a structure at equilibrium we may apply it to a cross-section of the active stomach at any instant. It relates to the circumferential tension, T, to transmural pressure, P_x , at a circular cross section, x, of radius r by the formula

LAW OF HOOKE

The force which empties the stomach is provided by gastric smooth muscle. Evans (1926) showed that smooth muscle has the property that the force generated in response to stretch is proportional to the proportional change in length. The constant of proportionality is called the tonus or tension, T, and is calculated as force per unit length. This fact was observed for the heart (Starling's law) and the stomach (Marbaix, 1898). It was shown by Brody and Quigley (1948a) that Hooke's law could be applied to a hollow organ of circular cross section r, and r_0 when resting, by the formula:

where a is constant and m is a constant variously taken as 0.0 (Winton and Bayliss, 1935), 1.0 (Brody

and Quigley, 1948a), and $2\cdot 0$ (Frank, 1910). The constant a contains the Young's modulus. This factor is presumably the biological coefficient which is influenced by the quality of the meal rather than its volume.

LAW OF POISSEUILLE

This has been applied to the stomach by Nelsen and Kohatsu (1971). It can be shown that

where $P = p_1 - k^2 p_2$ where 1 and 2 are points in a circular conducting pipe of radii $r = r_1 = kr_2$; 1 is the distance between points 1 and 2; p_1 and p_2 are pressures at 1 and 2; and n is the viscosity of the fluid flowing in the pipe.

THE ACTIVE STOMACH

The stomach contracts about three times every minute. We are concerned with its behaviour over a longer period than one minute and assume that the behaviour of the stomach over longer intervals can be treated as a smooth curve.

We may now combine these four assumptions to produce a model of gastric emptying.

Using eqn (A1) in the definition of P we have:

 $P = T_1/r_1 - k^2 T_2 r^2$ (A4)

since $r = r_1$ and $r = kr_2$ we have:

$$P = T_1/r - kT_2/r$$
 (A5)

Using eqn (A2) we have:

$$\mathbf{P} = \frac{a_1}{r} \left(\frac{r - r_0}{r^m} \right) r_0^{m-1} - \frac{a_2}{r} \left(\frac{kr - kr_0}{k^m r^m} \right)$$

$$(kr_0)^{m-1} \dots \dots \dots \dots \dots \dots (A6)$$

Hence:
$$\mathbf{P} = C_1 \left(\frac{\mathbf{r} - \mathbf{r}_0}{\mathbf{r}^{m+1}} \right) \mathbf{r}_0^{m-1} \dots \dots \dots \dots \dots (A7)$$

where $C_1 = a_1 - a_2$ (A8) Using eqn (A3) we have:

$$\frac{dV}{dt} = -\frac{\pi r^4}{8 \ln \eta} \frac{C_1(r - r_0) r_0^{m-1}}{r^{m-1}} \quad \dots \dots \quad (A9)$$

Hence:
$$\frac{dV}{dt} = -C_1 C_2 r^{4-m} \left(1 - \frac{r_0}{r}\right) r_0^{m-1}$$
 (A10)

where $C_2 = \pi/8l\eta$ (A11) Stomach geometry is complex and has been approximated to a sphere or a cone of fixed height, h. If 4 1

gastric volume is V then V = $\frac{4}{3}\pi r^3$ or V = $\frac{1}{3}\pi r^2h$ and

in general:

 $r = C_3 V^n$ (A12) where $0.33 \le n \le 0.50$, and C_3 is a constant. Substituting eqn (A12) into eqn (A10) we have (if v = volume at resting radius r_0):

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -\mathrm{C}V^{\mathrm{p}}\left(1-\left(\frac{\mathrm{v}}{\mathrm{V}}\right)^{\mathrm{n}}\right) \ldots \ldots (\mathrm{A13})$$

where $C = C_1 C_2 C_3^3 v^{n(m-1)} \dots (A14)$ and $p = n (4 - m) \dots (A15)$

From before we deduce that $1.00 \le p \le 1.33$.

Equation (A13) corresponds to equation (1) in the text. The exponents n and p have a geometrical basis and are best determined empirically. The constant, C, contains terms which are numerical, a function of gastroduodenal geometry, and a function of the composition of the meal which determines its viscosity and the value of the Young's modulus which the stomach assumes. We may presume that the contents of meals which act to slow gastric emptying do so by altering the Young's modulus ('contractility') of the stomach. The term C in equation (A13) is a function of the composition of the meal. The remaining terms in equation (A13) are functions of the volume of the meal.