MYOELECTRIC ACTIVITY OF THE STOMACH

GASTROELECTROMYOGRAPHY AND ELECTROGASTROGRAPHY

PROEFSCHRIFT

TER VERKRIJGING VAN DE GRAAD VAN DOCTOR IN DE
GENEESKUNDE
AAN DE ERASMUS UNIVERSITEIT ROTTERDAM
OP GEZAG VAN DE RECTOR MAGNIFICUS
PROF. DR. J. SPERNA WEILAND
EN VOLGENS BESLUIT VAN HET COLLEGE VAN DEKANEN
DE OPENBARE VERDEDIGING ZAL PLAATS VINDEN OP
WOENSDAG 4 JUNI 1980 DES NAMIDDAGS
TE 4.15 UUR

DOOR

ANDREAS JOHANNES PETRUS MARIA SMOUT
GEBOREN TE AMSTERDAM

DELFT UNIVERSITY PRESS / 1980

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aan Anja en Danielle

VOORWOORD

Aan het tot stand komen van dit proefschrift hebben zeer velen in belangrijke mate bijgedragen.
Allen ben ik zeer erkentelijk.

In het bijzonder wil ik alle (vaste en tijdelijke) medewerkers van de afdeling Medische Technologie der Erasmus Universiteit danken voor de uitermate plezierige en vruchtbare samenwerking.

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LIST OF ABBREVIATIONS USED

CP	Control Potential
ECA	Electrical Control Activity
ECP	Ectopic Control Potential
EGG	Electrogastrography
ERA	Electrical Response Activity
IDMEC	Interdigestive Myoelectric Complex
IMC	Interdigestive Migrating Complex
NECP	Nonectopic Control Potential

1. INTRODUCTION AND OBJECTIVES OF THE STUDIES

The musculature of the distal two-thirds of the stomach generates electrical signals that are related, in a complex manner, to the (peristaltic) contractions of these muscles. These electrical signals originate in ion shifts from the intracellular to the extracellular space and vice-versa.

Apart from recording *intracellular* electrical activity with the aid of a microelectrode inserted into the cell, gastric myoelectrical activity can be recorded in two ways.
Firstly, gastric electrical activity can be recorded with electrodes located in the immediate proximity of the muscle layers. This method is called *gastroelectromyography*. It provides information about the electrical activity of larger groups of cells.
Secondly, gastric myoelectrical activity can be recorded with the aid of electrodes at relatively large distances from the stomach (e.g. on the abdominal skin). This method is called *electrogastrography*. It provides rather global information about the electrical activity of the stomach.

Whereas the method of electrogastrography is still in a relatively early experimental phase, the method of *gastroelectromyography* has frequently been used in studies on gastric myoelectric activity, both in health and disease. The published descriptions of the characteristics on normal gastroelectromyographic signals are not in complete accordance, however. No agreement exists about the existence and meaning of the so-called 'second potential' (Daniel, 1965, 1966) and about the relation between intracellular and extracellular electrical activity.
Furthermore, gastroelectromyographic literature paid relatively little attention to the rhythm of the so-called 'Electrical Control Activity' (Sarna, 1975).

The literature on *electrogastrography* mainly consists of reports of attempts to diagnose gastric disorders with the aid of cutaneous recordings. In most of these attempts only external electrodes were used and no reference signals from the stomach itself were obtained. As a consequence, it is still unclear what exactly is measured in electrogastrography.
Furthermore, the characteristics of the (normal) electrogastrographic signals have not yet been described extensively.

This thesis deals with both *gastroelectromyography* (Chapter 4) and *electrogastrography* (Chapter 5).

Both in Chapter 4 and in Chapter 5 the major objectives of our studies were:
1. to answer the question 'what is measured?' and
2. to describe the characteristics of the recorded signals.

In most of our studies the *dog* was used as an experimental animal, since no significant difference between human and canine gastric myoelectric activity has ever been reported, neither with intracellular techniques, nor with gastroelectromyography, nor with electrogastrography.

In Chapter 5 the results of some electrogastrographic explorations in *man* will be described.

Both in Chapter 4 and in Chapter 5 purely observational studies will be described. The only stimulus applied to our dogs and human volunteers was the administration of food.
Answers to the question 'What is measured?' will be sought by comparing recorded gastroelectromyographic signals with intracellular signals known from literature and by comparing simultaneously recorded gastroelectromyographic and electrogastrographic signals.

In this thesis the electrical and mechanical activities of the proximal third part of the stomach (cardia, fundus and upper part of the corpus) will not be dealt with, since this part of the stomach does not generate electrical potentials that can be recorded extracellularly.

2. ANATOMY OF THE STOMACH

2.1 *Macroscopic anatomy*

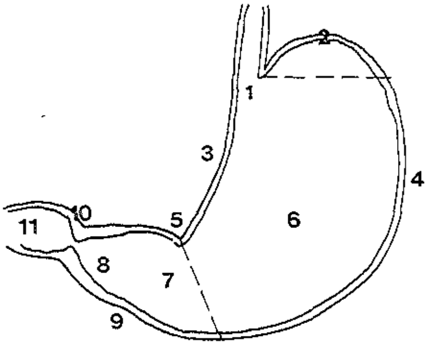

*Fig.1 Macroscopic anatomy of the stomach.
For explanation of numbers see text.*

The cardiac portion (or cardia)[1] is that part of the stomach that surrounds the gastroesophageal orifice. The fundus[2] is the part oral to the gastroesophageal junction.

The concave right border of the stomach is called the lesser curvature[3], the left border, which is five times as long, is the greater curvature[4]. In the lesser curvature a notch is present, the angular incisure[5]. The plane through the angular incisure and perpendicular to the longitudinal axis of the stomach separates corpus[6] and pyloric portion[7+8]. The pyloric portion is divided into a proximal part, the pyloric antrum[7], and a distal part, the pyloric canal[8]. The boundary between these parts is sometimes indicated by a shallow indentation of the larger curvature, the sulcus intermedius[9]. In the pyloric canal (length 2 to 3 cm) the circular muscle layer thickens to what has been called an intermediate sphincter (Torgersen, 1942).

The junction between stomach and duodenum[11], the pyloric sphincter or pylorus[10], is also characterized by a thickening of the circular muscle layer. According to some publications a hypomuscular segment is present immediately aboral to the pyloric sphincter (e.g. Bass et al., 1961).

The term 'antrum' is often used as a synonym for pyloric portion. In this thesis this will likewise be done.

The term 'terminal antrum' is often used, by others and by ourselves, as a synonym for pyloric canal.

The gastric wall, like the wall of most other parts of the digestive canal, consists of four main layers (Fig.2).

From outside inwards, a serosal layer[1], a muscular layer[2] consisting of an outer longitudinal and an inner circular layer, a submucosal layer[3], and a mucosal layer[4] are encountered. In the stomach a very incomplete oblique muscular layer is present under the circular muscle layer.

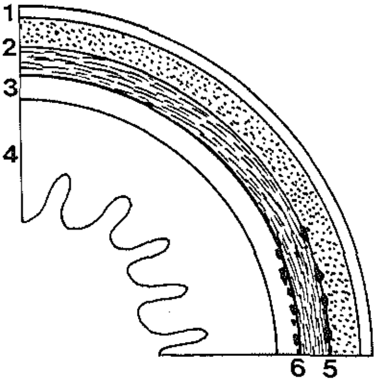

Fig.2 Scheme of the layers of the wall of the digestive canal.
For explanation of numbers see text.

All layers contain nerve plexuses. The most important plexuses are the myenteric plexus of Auerbach[5], situated between the longitudinal and the circular muscle layers, and the submucosal plexus of Meissner[6], situated underneath the circular muscle layer.

The muscle layers will now be described in some more detail.
The *longitudinal layer* is the most superficial muscle layer, situated directly under the serosa. A group of fibers is continuous with the longitudinal layer of the esophagus; these fibers run along the curvatures and end in the corpus (Fig.3).

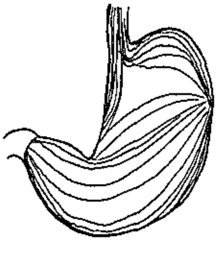

Fig.3 Longitudinal muscle layer.
(After Weber and Kohatsu, 1970).

A second group of longitudinal fibers originates in the corpus at the greater curvature. These fibers radiate in all directions, but in particular towards the pylorus.
The point of origin at the greater curvature has been regarded as the anatomical correlate of the electrical pacemaker region, to be discussed in chapter 4.2.3 (Weber and Kohatsu, 1970).
A part of the longitudinal fibers passes over the pylorus into the longitudinal muscle layer of the duodenum.

The *circular layer* (Fig.4), the middle of the three layers, is continuous with the circular layer of the esophagus. It is absent over the fundus. The thickness of the circular layer increases in the antrum and especially in the pyloric canal. The circular muscle fibers are alleged not to be continuous with the circular fibers of the duodenum.

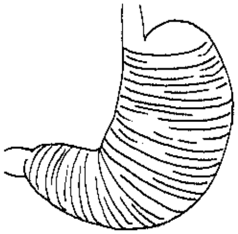

Fig.5 Circular muscle layer.

The *oblique layer*, the innermost layer, has the shape of a horse-shoe hanging over the fundus (fig.5). On the right side (near the lesser curvature) the borders of this layer are sharply defined, on the left side and towards the antrum the oblique fibers disappear gradually.

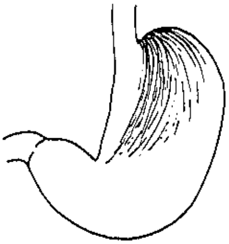

Fig.5 Oblique muscle layer.

2.2 *Microscopic anatomy of intercellular contacts between gastric smooth muscle cells.*

Around the last turn of the century it became the vogue to suppose that the cytoplasmata of neighbouring smooth muscle cells were in direct contact; in other words, that smooth muscle cells formed a syncytium. At the end of the fifties more delicate electron microscopic techniques made it possible to establish that continuity of cytoplasm of different cells does not occur in smooth muscle.

Since 1960 however, a considerable amount of studies about cell-to-cell contacts in smooth muscle has been published. Several types of intercellular structures, creating close contacts between neighbouring cells, have been described.

The terminology used for these structures is rather confusing.

Furthermore, there is still some dispute about which structures should be considered artifacts and which not. The following is a summary of the generally accepted types of intercellular contacts in smooth muscle. More detailed information can be found, e.g., in the surveys by Burnstock (1970) and Henderson (1975).

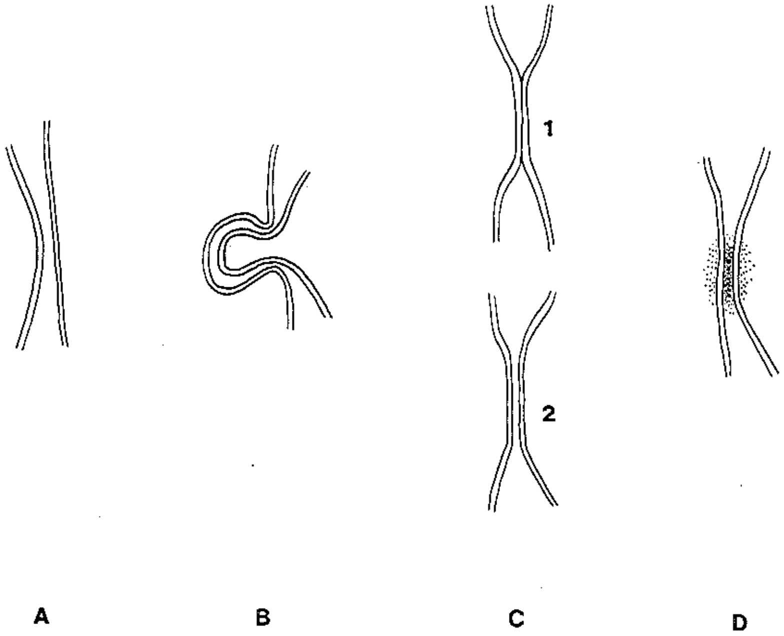

Fig.6 Intercellular contacts (schematic).

The following types of intercellular contacts can be distinguished:

A. *'Close appositions'* (Fig.6A). These are areas in which the membranes of two cells are very near to each other. The intercellular cleft is about 10 to 20 nm (100 to 200 Å) wide.

B. *'Intrusions'* ('interdigitations, peg-and-socket structures'). This type of contact is characterized by an evagination of the cell fitting in an invagination of another cell (Fig.6B). This type of contact can be observed in combination with a gap junction (C).
Daniel et al. (1976) are of opinion that peg-and-socket structures are produced by swelling of cells during fixation.

C. *'Gap junctions' or 'nexuses'* (Fig.6C) are areas in which the membranes of neighbouring cells approach each other to a distance of bout 2 nm. Depending on the method of preparation a 5-layered (Fig.6C$_1$) or a 7-layered (Fig.6C$_2$) sandwich structure is seen. In the former case the outer leaflets of the two adjoining membranes appear to be fused.

D. *'Intermediate junctions'* ('desmosome-like attachments') are areas in which the narrow intercellular gap is filled with dense material and in which the cytoplasm under the membranes is denser than usual.

It is supposed that the above intercellular contacts form pathways of low electrical impedance for the currents involved in the excitation and synchronization of smooth muscle cells. Particularly the nexuses have been regarded as essential for electrical coupling (e.g. Dewey, 1965). Direct evidence for these assumptions is absent.

Gap junctions (nexuses) are present in great numbers in the circular muscle layer of the electrically active parts of the canine stomach.
In the electrically inactive part of the stomach and in the longitudinal muscle layer gap junctions are almost absent (Daniel et al., 1976). Since the longitudinal layer does show signs of electrical coupling, it can be concluded that gap junctions are not necessary for coupling.
Both in the longitudinal and in the circular layers of the canine stomach close appositions are frequently observed. Intermediate junctions are rare (Daniel et al., 1976).

3. INTRACELLULAR ELECTRICAL ACTIVITY OF GASTRIC SMOOTH MUSCLE
(Literature survey)

3.1 Introduction

The membrane potential can be recorded with a *microelectrode* inserted into the cell. Because of the small dimensions of smooth muscle cells this technique is difficult. As a consequence, only three groups of investigators published results of microelectrode studies on gastric smooth muscle. However, signals resembling (but not equal to) those obtained with microelectrodes can be obtained with the following *extracellular* techniques:
- the pressure electrode technique,
- the suction electrode technique and
- the sucrose-gap technique.

The pressure and suction electrode techniques have been applied to gastrointestinal smooth muscle in particular by Bortoff (1961a, 1961b, 1967, 1975a). The mechanism underlying these two techniques is probably the same one; the cell membrane underneath the electrode depolarizes, the membrane resistance decreases and the electrode 'sees' through a hole in the membrane into the interior of the cell.

The sucrose-gap technique has been used by several groups working on gastrointestinal smooth muscle. In this method the potential difference between an extracellular electrode over a constantly depolarized area and an electrode over an active area is measured, while the area in between is washed with a (non-conductive) sucrose solution.

For detailed treatments of these pseudointracellular techniques the reader can be referred to Bortoff (1967, 1975a) and Coburn et al. (1975) respectively.

It should be noted that with pressure electrodes, with suction electrodes and with the sucrose-gap method the activities of many cells at a time are recorded and that only the microelectrode technique offers the possibility to record the intracellular electrical activity of a single cell.

Almost all information about the intracellular electrical activity of gastric muscle comes from in vitro studies on muscle strips.

In vivo measurements with microelectrodes were performed only by Daniel (1965) (canine antrum).

The muscle strips used, either contain all muscle layers (as far as present), or consist solely of longitudinal or circular muscle fibers. However, 'when examined histologically, the "longitudinal strip" usually contains myenteric plexus as well as the outermost layer of circular muscle' (Daniel and Sarna 1978).

Both longitudinal and circular strips of the stomach of dog, man and guineapig generate action potentials spontaneously (Szurszewski, 1975, El-Sharkawy et al., 1978, Ohba et al., 1975, 1977). These findings are in contrast with the conclusion drawn by Papasova et al. (1968) that the circular layer is not spontaneously active and that this layer is driven by the longitudinal layer. Possibly, differences in preparation technique account for this discrepancy in the literature.

3.2 Frequencies of action potentials in gastric muscle strips

The repetition frequencies of the action potentials[x)] generated by strips of gastric muscle are lower than the frequency of the electrical activity of the intact stomach, both in vivo and in vitro.
In the dog this latter frequency is about 5 cycles per minute (cpm). In circular strips taken from the canine stomach El-Sharkawy et al. (1978) found a decrease in action potential frequency from corpus to pylorus; proximal corpus 3.7 ± 0.1 cpm, distal corpus 3.5 ± 0.1 cpm, pyloric antrum 1.4 ± 0.1 cpm, terminal antrum 0.66 ± 0.1 cpm and pyloric ring 0.15 ± 0.03 cpm.
Intrinsic frequencies in muscle strips taken from the human stomach have been found to be higher than the in vivo frequency of the intact human stomach (which is about 3 cpm) (El-Sharkawy et al., 1978). The relevance of this finding is yet unclear.

3.3 Configurations of action potentials of gastric muscle

The action potential generated by the smooth muscle of the distal two-third part of the stomach of cat, dog and man can be described as consisting of four parts (Fig.7):

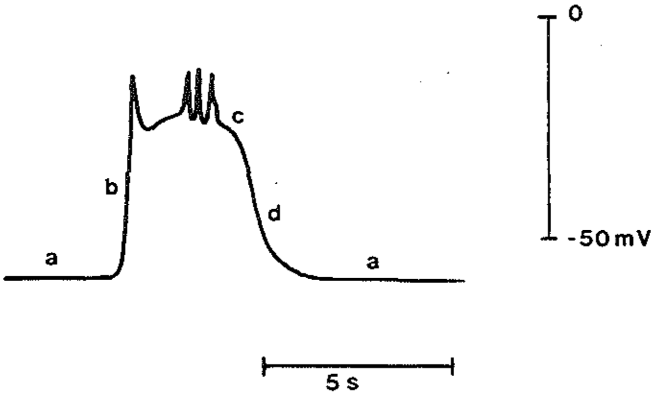

Fig.7 Configuration of the action potential generated by gastric smooth muscle cells.

a = resting membrane potential
b = depolarization phase
c = plateau phase, which may or may not bear spikes
d = repolarization phase

It should be noted that the smooth muscle of the proximal third part of the stomach does not generate these action potentials. The electrical activity of this gastric part will be discussed briefly in Chapter 3.4..

[x)] Here, the term 'action potential' is used to denote one cycle of depolarization and repolarization of the cell membrane, as recorded intracellularly.

Moreover, it should be noted that the term 'action potentials' is used by some investigators to denote extracellularly recorded spikes. It must be emphasized that the characteristics of the action potentials to be described here, concern gastric smooth muscle of dog, cat and man, unless stated otherwise. Because of the considerable diversity in smooth muscle, the described characteristics cannot be extrapolated to other types of smooth muscle or to other species.

3.3.1 Resting membrane potential

Resting membrane potentials of about -70 mV have been found in circular muscle cells of the canine stomach (El-Sharkawy et al., 1978). The same investigators found similar values in human gastric muscle cells.

'Diastolic depolarization' is a term used by cardioelectrophysiologists to denote the phenomenon of gradual decrease of the resting membrane potential between consecutive action potentials of cardiac muscle cells. It is assumed that heart cells not exhibiting diastolic depolarization are unable to function as a pacemaker cell, i.e. to generate action potentials spontaneously.
In muscle strips from the corpus of the canine stomach the phenomenon of diastolic depolarization was found to be present in 89% of the cases, whereas in the distal part of the corpus and in the antrum the phenomenon was rare (El-Sharkawy et al., 1978). Noradrenaline and pentagastrin induce diastolic depolarization in the antrum (circular layer, canine stomach) (El-Sharkawy and Szurszewski, 1978).

3.3.2 Depolarization phase

This phase has also been named *initial depolarization phase, first component, spike component* and *upstroke potential.*
In order to avoid confusion, only the term depolarization (phase) will be used in this thesis.

Measured with intracellular electrodes the amplitude of the depolarization increases in the direction of the pylorus. In canine circular muscle El-Sharkawy et al. (1978) found mean amplitudes of 28.5 mV in the corpus, of 45.8 mV in the pyloric antrum, of 61.4 mV in the pyloric canal, and of 73.8 mV in the pyloric sphincter. By the same investigators lower depolarization amplitudes were found in man, but conclusions with regard to the existence of an amplitude gradient in man can not yet be drawn. Lower depolarization amplitudes have been measured with the sucrose-gap method: about 20 mV in antral muscle (Papasova and Boev, 1976; Szurszewski, 1975).

Like the amplitude, the depolarization rate (dV/dt) also increases from corpus to pylorus. With microelectrodes, values of 0.54 V/s in the corpus to 2.15 V/s in the pylorus have been found (El-Sharkawy et al., 1978). With the sucrose-gap technique lower values are found (Szurszewski, 1975).

The configuration of the depolarization phase is relatively constant. It is generally accepted that there is no relation between the configuration of the depolarization and the contraction that may *or may not* follow it. Put otherwise; the depolarization phase seems not to determine whether or not a contraction will take place.
Only Papasova and Boev (1976) are of opinion that the velocity of depolarization is higher when the action potential leads to a con-

traction.

In the gastric antrum of rat, mouse and guinea-pig the depolarization phase is much slower, almost as slow as the repolarization phase, leading to a 'sinusoidal' action potential configuration (Milenov and Boev, 1972; Golenhofen et al., 1970; Boev, 1972). (Fig.8, left part.)
In contrast, Ohba et al. (1975, 1977) found relatively rapid depolarizations in the antrum of the guinea-pig. The presence of a hump in the depolarization gave rise to a description in which a lower and an upper component are distinguished (Fig.8, right part).

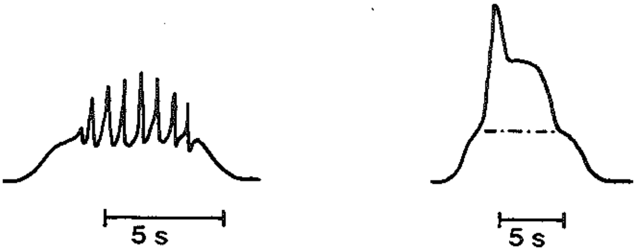

Fig.8 Left : Configuration of action potential of antral smooth muscle in guinea-pig. Sucrose-gap technique. (After Golenhofen et al.1970)

Right: Configuration of action potential of antral smooth muscle in guinea-pig. Sucrose-gap technique. (After Ohba et al.1975, 1977)

3.3.3 Plateau phase

This phase has also been called *second component* or *prolonged depolarization*. In this thesis the term plateau (phase) will be utillized only.
The transition between depolarization and plateau usually consists of a partial repolarization.

In mechanically inactive tissue, the plateau is completely absent (Papasova et al., 1968; Daniel, 1965), or of small amplitude and duration (Szurszewski, 1975).
Papasova and Boev (1976) reported that the contractile force (measured isometrically) appeared to be related with (to depend on?) the amplitude of the plateau.
The results of studies on the effects of acetylcholine, noradrenalin and pentagastrin on intracellular signal and contractile force, performed by Szurszewski and co-workers (Szurszewski, 1975; El-Sharkawy et al., 1978), corroborate Papasova and Boev's report (Fig.9).

Stronger contractions appear to be associated with higher plateaus and with plateaus of longer duration. The duration of the strongest contraction in Fig.9 is unusually long in comparison with the phasic contractions shown in other publications. It is not clear whether this is due to an additional activation of the tonic contractile mechanism, or to the technique used to record contractile force.

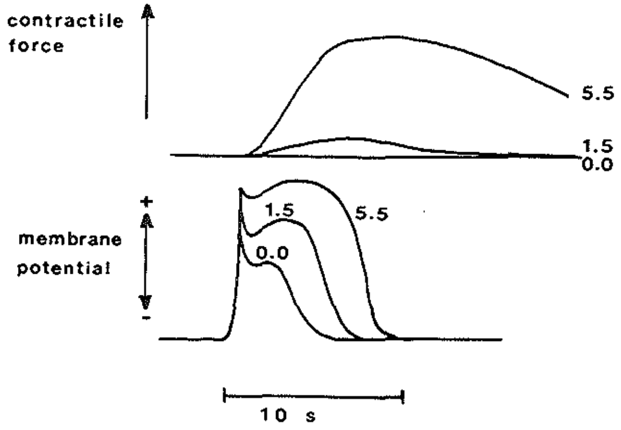

Fig.9 Relation between configuration of intracellular electrical signal and contractile force. The tissue was stimulated with acetylcholine; the figures indicate the acetylcholine concentration (× 10^{-8} M) in the bathing solution. After Szurszewski (1975). Longitudinal layer of canine antrum, sucrose-gap.

Very recently, Szurszewski and co-workers reported the existence of 'biphasic' contractions, the first phase of which seems to be elicited by the depolarization (Sanders and Szurszewski, 1979; Szurszewski pers.comm., 1979). As illustrated in Fig.10, these reports imply that *complete* mechanical inactivity, formerly believed to accompany action potentials without plateau, does not occur. It should be noted, however, that the depolarization-related contractions are very weak (and therefore are missed at normal sensitivity of the recording apparatus). It is considered to be very unlikely that these contractions cause any movement or exert any force at the level of the mucosa.

Spikes, if present, are superimposed upon the plateau.

In the literature on intracellular electrical activity agreement exists about the fact that *phasic contractions can occur without spiking*. According to most authors in this field, the incidence of spikes is highest in the most distal part of the stomach. Papasova et al. (1968), however, stated that 'spiking was especially prominent in records from the cardiac end'.

Smooth plateaus can be converted into plateaus with spikes by adding tetraethylammonium (TEA) to the bathing solution (El-Sharkawy et al., 1978). The mechanism underlying this effect is yet unclear.

El-Sharkawy et al. (1978) described the presence of a transition zone between the zone with smooth plateaus (taking up more than half of the stomach) and the zone of spike-bearing plateaus (usually confined to the pyloric canal). In this transition zone no spikes, but only oscillations are present on the plateau.

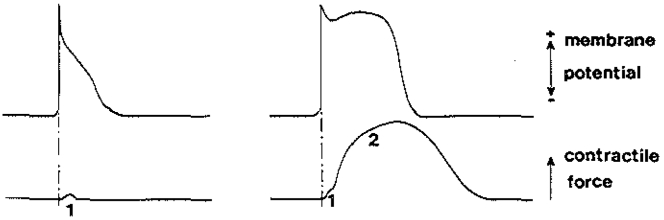

Fig.10 The two phases of phasic contractile activity in gastric smooth muscle, according to Szurszewski and co-workers (schematic).

Left : no plateau present; only a tiny, depolarization-related contraction (1) is seen.

Right: both a depolarization-related (1) and a plateau-related (2) contraction are present, resulting in a 'biphasic' contraction configuration.

These zones were observed both in the canine and in the human stomach. According to Bortoff (1975b), spiking is more frequent in the cat stomach than in the canine stomach.
In the stomach of rat, mouse and guinea-pig spike-free initiation of phasic contractile activity was not observed by Golenhofen et al. (1970) and Boev (1972); only when spikes were superimposed upon the sinusoidal action potentials, contractions occurred. In this respect the stomachs of these rodents show much resemblance to the small intestine of many species, including dog and man. Spike-free initiation of phasic contractile activity appears to be a rather unique property of the smooth muscle of the stomach of dog, cat and man.

According to Daniel (1965), the intracellular signal usually exhibits a small secondary depolarization, following a partial repolarization and preceding the plateau (Fig.11).

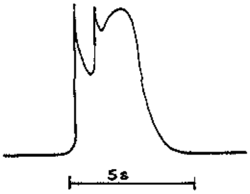

Fig.11 Secondary spike-like depolarization. After Daniel (1965). Canine antrum.

In the remaining literature such a secondary depolarization is not mentioned, nor depicted.

The duration of the plateau was measured by El-Sharkawy et al. (1978). Values of 5.9 ± 0.2 seconds in the corpus to 11.3 ± 0.2 seconds in the terminal antrum were found. Since the degree of contractile activity of the studied strips is not communicated, these values are of limited significance.

3.3.4 Repolarization phase

In the literature, this phase got little interest.
It is important, however, to note that a high amplitude of the plateau is correlated with a high velocity of repolarization (see Fig. 9). This fact will be used in the Chapters 4 and 5.

3.4 Intracellular electrical activity of fundic smooth muscle cells

The smooth muscle cells of cardia, fundus and upper part of the corpus do not generate action potentials as described in the preceding paragraphs. At the same time these cells are not capable of executing phasic contractions. In the most proximal parts of the stomach only very slow, tonic contractions occur.
Recently, evidence has been presented that these tonic contractions are accompanied with slow, partial depolarization of the cell membrane (Boev et al., 1976; Morgan and Szurszewski, 1978; Morgan et al., 1979). This change in membrane potential is probably too slow and too small to give rise to extracellular potential changes; in reports of studies with extracellular electrodes the most proximal part of the stomach is described as electrically silent.
The resting membrane potential of fundic smooth muscle cells is somewhat lower than that of the muscle cells in the rest of the stomach: -58 mV (El-Sharkawy et al., 1978).

4. GASTROELECTROMYOGRAPHY

4.1 Introduction

The term 'gastroelectromyography' or 'electromyography of the stomach' can be used to denote the method of recording gastric myoelectric signals with extracellular electrodes of which at least one is in the immediate proximity of the muscle layers.
In the literature the term 'electrogastrography' has been used to denote the above-mentioned method. It seems preferable however, to reserve the term electrogastrography for the recording technique that employs remote electrodes (e.g. on the skin). This because of the analogy with terms as electrocardiography and electroencephalography.

The first gastroelectromyograms were recorded with string galvanometers, about 1920.
One of the pioneers in this field was Walter Alvarez, who worked in San Francisco. Most of his observations, made with very primitive apparatus, deserve great admiration (Alvarez, 1922a, 1922b).
The same can be said about Curt Richter's description of "Action currents from the stomach' (Richter, 1924). Many of the phenomena described by Alvarez and Richter have been rediscovered by later investigators. It seems that little progress has been made in the field of gastroelectromyography between 1925 and 1960.
Since 1960 an enormous increase in interest in the topic has occurred, manifesting itself in a growing stream of publications on the subject.

4.2 Literature survey

4.2.1 Techniques of recording gastroelectromyographic signals

The following survey of gastroelectromyographic techniques will be confined to methods applicable *in vivo*.

1. Firstly, a distinction must be made between *monopolar (unipolar)* and *bipolar* recording techniques.
   In the case of monopolar recording, one of the electrodes (called the 'exploring', 'active', or 'different' electrode) is in the immediate proximity of the smooth muscle, and the other electrode (the 'reference', the 'neutral', or 'indifferent' electrode) is as remote as possible. In most in vivo experiments the indifferent electrode is placed in or on the right hind leg of the experimental animal.
   In the case of bipolar recording both electrodes are positioned close to another, in or near the muscular layer (Fig.12).
2. The muscle layers of the stomach can be approached from the *serosal* side or from the *mucosal* side.
   In case of a *serosal approach* one can use electrodes that do not penetrate the serosa (e.g. McCoy and Bass, 1963), electrodes to be positioned directly under the serosa (e.g. Daniel and Chapman,

1963), or electrodes to be inserted into the muscularis. This last technique has been applied most frequently. It is also the technique used by ourselves.
In case of a *mucosal approach* the electrode(s) are mounted in or on a catheter which is swallowed. Mostly the tip of the catheter is kept in position by means of suction. The electrodes either penetrate the mucosa (e.g. Kwong et al., 1970), or are just pushed against it (e.g. Civalero and Kanteliu, 1978).
The signals obtained with mucosal electrodes show much resemblance to those obtained with serosal electrodes.

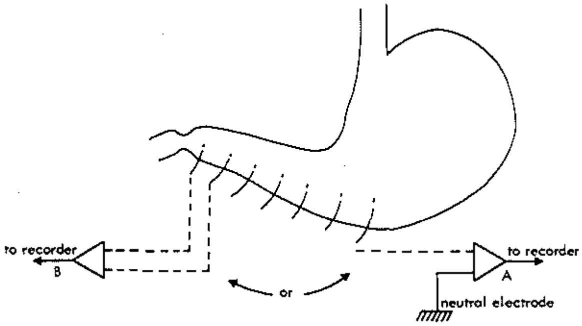

Fig.12 Monopolar (A) and bipolar (B) gastroelectromyography.

3. Various *materials* and *configurations of electrodes* have been used. Most often, chlorided silver is chosen as electrode material. Such for its well-known favourable properties (low impedance, low noise). Other materials that have been used are platinum (e.g. Papasova et al., 1976), stainless steel (e.g. Kwong et al., 1970), and vitreous (glassy) carbon (Kingma, 1977).
   The configuration of the electrode particularly depends on the chosen way of approach (see 2).
   A frequently employed type of serosal electrode consists of a pointed silver wire, protruding 2 to 3 mm from a small plate (e.g. Kelly et al., 1969).
4. Finally, it should be pointed out that different authors use different *filtering* while recording gastroelectromyographic signals. Although it is obvious, in theory, that a frequency range as wide as possible should be let through by the filters, it turns out that, in practice, rational and irrational deviations from this basic rule occur frequently.

4.2.2 Techniques of recording gastric contractile activity

Although the mechanical activity of the stomach is not the main subject of this thesis, it seems necessary to discuss briefly the most frequently used techniques of recording gastric contractile activity. Again, the survey will be confined to methods applicable in vivo.

1. A relatively simple method is the *direct visual observation* of the movements of the stomach. A survey of the earliest observations,

including those on patients with large gastric fistulas, was provided by Alvarez (1968).

2. *Fluoroscopy* of the contrast liquid containing stomach is a method that can furnish clear pictures of the gastric movements. The method has the following disadvantages:
   - dangerous dosages of radiation are used, limiting the observation time,
   - the results are difficult to quantify,
   - observations on fasting subjects are not possible.
3. *Measurement of intragastric pressure,* though often employed, is a method with obvious limitations. When open-tip catheters or small balloon catheters are used, smaller contractions, not leading to compartimentalization of the stomach, can be missed (Code and Carlson, 1968). Larger, fluid-filled balloons exhibit this drawback to a lower degree, but 'act as a stretch stimulus and induce a contraction response or resistance to stretch which is recorded as "tone"' (Edwards and Rolands, 1968).
4. *Extraluminal measurement of contractile force* or *displacement.*
   a) The extraluminal force transducers developed by Bass and coworkers (see e.g. Jacoby et al., 1963; Bass and Wiley, 1972) have gained much popularity. This type of transducer consists of two metal foil strain gauges mounted in a silicone rubber housing (Fig.13).

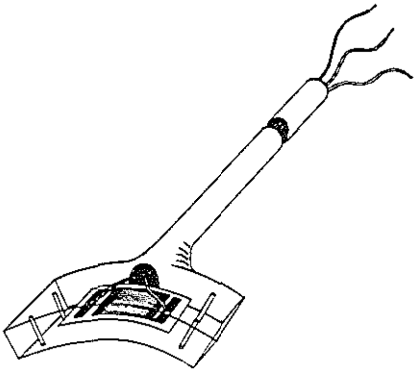

Fig.13 Extraluminal strain gauge force transducer as developed by Bass and co-workers.

The transducer is sutured to the serosal surface of stomach or intestine, mostly in a transverse direction, so that circular contractions are measured. The force exerted by the contracting tissue results in some bending of the transducer. By this bending the upper strain gauge is stretched and the lower is upset. The resulting resistance changes are converted into potential changes in a Wheatstone bridge.

Since this type of transducer is rather stiff, the underlying muscle performs approximately isometric contractions (unlike the rest of the muscle). The transducer is suited for use in chronic experiments.

Nowadays, semiconductor strain gauges are also used in the construction of extraluminal force transducers. With these strain gauges smaller transducers can be manufactured (e.g. Hubel and Follick, 1976).

b) Displacement transducers, enabling the measurement of the shortening of isotonically contracting tissue, found much less application (in our field) than the above-mentioned force transducers. A group in Strasbourg developed implantable displacement transducers working with strain gauges (e.g. Mendel et al., 1979). An inductive transducer for use on the stomach has been described by Kingma et al. (1975).
From a theoretical point of view, displacement transducers are often preferable to force transducers. The major disadvantage of displacement transducers, however, is that they are not suitable for prolonged chronic experiments; some time after implantation fibrous tissue forms a more or less rigid bridge between the moving parts of the transducer.

4.2.3 Characteristics of serosal gastroelectromyographic signals in the dog (as described in the literature)

Every 10 to 12 seconds a change in potential, called 'pacesetter potential' by the group of investigators working at the Mayo Clinic (Code et al., 1968; Kelly et al., 1969; Kelly and Code, 1969, 1971; Kelly and La Force, 1972), and 'initial potential' by Daniel (Daniel, 1965, 1966; Daniel and Irwin, 1968), originates in the orad corpus and subsequently travels towards the pylorus (Fig.14).

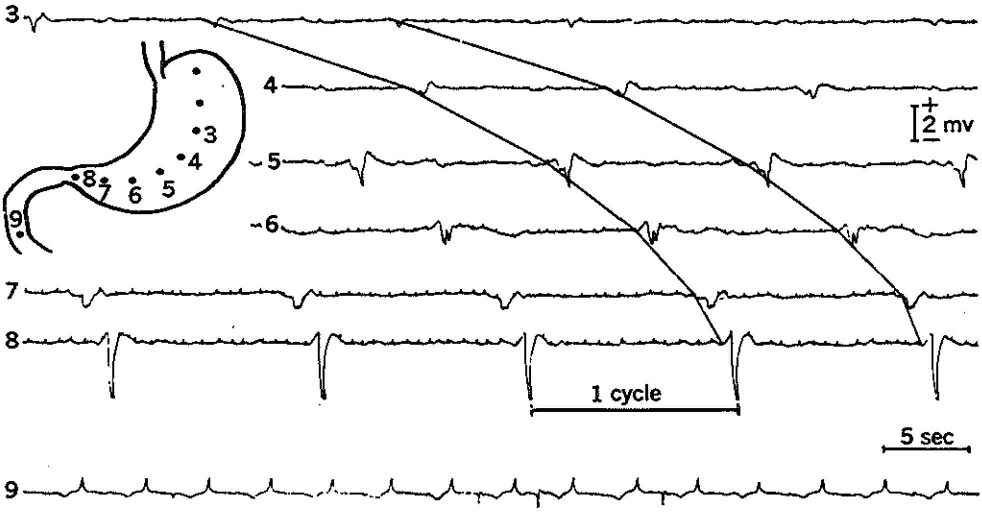

Fig.14 Signals recorded from monopolar serosal electrodes on the anterior surface of the canine stomach. Electrode 8 is located 1 cm orad to the pylorus, the distances between the electrodes are approximately 3 cm. The most proximal portion of the stomach is electrically inactive. Fasting conscious dog. From Code et al., 1968.

When recorded with monopolar electrodes, the configuration of the propagating potential fluctuations is more or less triphasic. The main deflection is negative however.

The amplitude of this latter deflection is greater in the antrum than in the corpus; 2.8 and 0.8 mV respectively (Kelly et al., 1969).

The velocity of propagation increases in the direction of the pylorus; from 0.1 - 0.2 cm/s in the orad corpus to 1.5 - 4 cm/s in the antrum (Daniel and Irwin, 1968).

As a consequence of the slow propagation velocity with respect to the cycle duration, more than one triphasic complex is present on the stomach at any time. In Fig.14 (from Code et al., 1968) three complexes are present at a time; this is not a typical situation, since in most dogs the most proximal site from which the complexes could be derived was electrode 4 (Kelly et al., 1969).

These triphasic complexes (pacesetter potentials, initial potentials) can *always* be recorded, *whether the stomach is mechanically active or not.*

During episodes of motor quiescence the segments of the signals between the triphasic complexes are isoelectric or nearly isoelectric.

When phasic contractions occur, potential changes take place in the first part of the isoelectric segment, just after the triphasic complex.

With regard to the characteristics of these contraction-related potential changes, differences of opinion are encountered.

In the description by Daniel and Irwin in the Handbook of Physiology (1968) it says: 'In the contracting stomach, a second electrical deflection (the "second potential") is seen on conventional monopolar records... The second potential is typically recorded as a prolonged (4 - 8 sec.) negative deflection; it may, however, be a series of negative spikes. Spikes are usually seen only in the terminal 2 or 3 cm of the dog antrum.' In contrast, the description by Kelly et al. (1969) reads: 'Simultaneous recordings of electrical events, the changes in intragastric balloon pressure, and motility as seen fluoroscopically showed that contractions occurred only when action potentials (= spikes) were recorded... They (the spike bursts) always occurred during the second portion of the PP (pacesetter potential) cycle, just after the triphasic complex, and were usually accompanied by a monophasic, negative deflection.'

These descriptions might give rise to the inference that in monopolar gastroelectromyography three types of contraction-related potential changes can be distinguished (Fig.15).

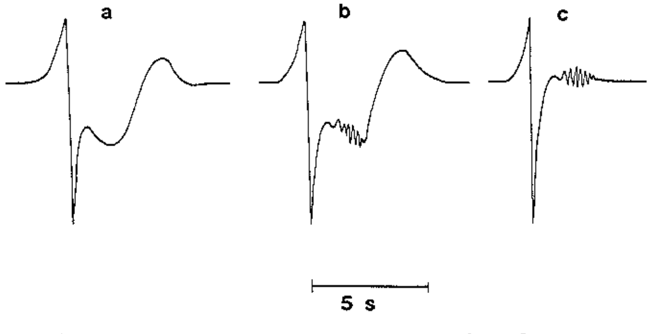

Fig.15 The three types of contraction-related potential changes in monopolarly recorded signals described in the literature.
a = second potential without spikes; c = spikes without second potential.
b = second potential plus spikes;

It should be noted that type c (spikes without second potential) was drawn on the basis of *descriptions* only (e.g. Kelly et al., 1969), since spikes without second potential could not be found in any of the *illustrations* in the publications cited above.

A histologically identifiable group of pacemaker cells, as in the sinoatrial node of the heart, has never been described in the stomach. Attempts to localize the pacemaker by means of gastroelectromyography of the intact stomach fail because of the fact that the amplitude of the initial potentials decreases in oral direction.
All conclusions regarding the localization of the gastric pacemaker were drawn from experiments in which the muscle layers of the stomach were transected. Following a transection of the muscularis, the frequency of the initial potentials orad to the transection remains unchanged, whereas in the distal segment a frequency drop occurs (Milenov, 1968; Weber and Kohatsu, 1970; Kelly and Code, 1971; Bedi et al., 1972; O'Leary and Hennessy, 1977; Hinder and Kelly, 1977). These experiments led to the conclusion that the pacemaker is situated on the greater curvature, somewhere in the orad corpus (Weber and Kohatsu, 1970; Kelly and Code, 1971).
Weber and Kohatsu (1970) are of opinion that 'anatomical studies of the gastric longitudinal muscle support the localization of the gastric pacemaker as defined by these studies of electrical activity'. According to these authors the region on the greater curvature where a group of longitudinal fibers originates, is the anatomical correlate of the pacemaker area.

The phenomena observed after transection of the gastric muscularis gave rise to a model introduced by Sarna, Daniel and Kingma, in which the initial potentials are regarded as the output of an array of *bidirectionally coupled relaxation oscillators* (Sarna et al. 1972a, 1972b and 1972c).
The intrinsic frequencies of the oscillators used in the model decline towards the pylorus, such on the basis of the results of transection experiments. In the coupled state, the oscillator with the highest intrinsic frequency (the most proximal oscillator of the array) leads all distal oscillators. In the coupled state, 'phase differences' occur between the oscillators. Phase differences similar to those found in reality can be obtained by choosing suitable values for the coupling factors between the oscillators.

As indicated above, the relaxation-oscillator-model has its own terminology. In this thesis we will use the terminology of the 'classical' model (in which initial potentials arise in a pacemaker area and 'travel' towards the pylorus).

4.2.4 *Nomenclature regarding gastroelectromyographic signals*

Many names have been given to the omnipresent periodic potentials and the contraction-related potentials described in the previous chapter. Most of these terms were created without considering the relations between the extracellular potential variations to be described with them and the intracellular electrical activity.

The *omnipresent, periodically occurring potential change,* recorded with monopolar techniques as a more or less triphasic complex, has been named:
- *initial potential* (Daniel, 1965, 1966; Daniel and Irwin, 1968)
- *pacesetter potential* (PSP or PP) (Code et al., 1968; Kelly etal., 1969)

- *q- and k-wave* (Richter, 1924)
- *first component* (Papasova et al., 1968)
- *control potential* (CP) (Sarna et al., 1972b; Sarna and Daniel, 1973; Sarna, 1975)

In addition, the whole of these rhythmically recurring potentials, propagating over the stomach, has been termed:

- *basic electrical rhythm* (BER) (Bass et al., 1961; Carlson et al, 1966)
- *electrical control activity* (ECA) (Sarna et al., 1972a; Sarna, 1975)

Furthermore, one may encounter the terms

- *slow wave(s)* (e.g. Papasova et al., 1968), and
- *control wave(s)* (Sarna, 1975).

The *slow contraction-related deflection* has been designated:

- *w-wave* (Richter, 1924)
- *second potential* (Daniel, 1965, 1966; Daniel and Irwin, 1968)
- *second (slow) component* (Papasova et al., 1968)

The *fast contraction-related oscillatory deflections* have been described with the terms:

- *spikes* or *spike potentials* (e.g. Papasova et al., 1968)
- *fast activity* (Allen et al., 1964; Bass et al., 1961)
- *action potentials* (AP) (Kelly et al., 1969; Code et al., 1968)
- *electrical response activity* (ERA) (Sarna et al., 1972A; Sarna, 1975).

Each of these terms has his pros and cons, most of which have been put forward in the literature.
The terms 'control potential' and 'electrical control activity' point at a controlling function of the initial potential. This controlling function is strongly suggested by the observations that spikes, second potentials and phasic contractions only occur in a specific phase of the control wave cycle. The impression of a controlling function becomes even stronger when the stomach as a whole is considered and it is observed that the phasic contractions (if present) always travel at the rear of the initial potentials. It seems that, by determining the times of occurrence of the contractions, the initial potentials determine the direction of propagation and the propagation velocity of the contractions.
It should be realized, however, that initial and second potentials, as well as spikes, are extracellular correlates of intracellular electrical activity. It is very unlikely that the extracellularly recorded potential variation which has been called 'control potential' actually controls something itself.

In this thesis we will use the terms:
- *initial potential*,
- *second potential*,
- *spikes*,

- *electrical control activity* (ECA),
- *electrical response activity* (ERA), and
- *control potential* (CP).

It is stressed that we will use the term ERA in a sense different from the one meant by Sarna. Whereas in the publications by Sarna and colleagues the term ERA is used as a synonym of spike activity (Sarna, 1975), we will use it to designate both second potentials *with* and second potentials *without* spikes.

4.2.5 *Interdigestive and digestive patterns*

4.2.5.1 *Interdigestive patterns*

In 1969 Szurszewski described the migrating electrical complex observed by him in the small intestine of the fasting conscious dog. Episodes of intense spike activity (activity fronts) appeared to arise in the duodenum and to propagate slowly (in 115 to 183 minutes) to the terminal ileum.
In 1975 Code and Marlett published an extensive description of this interdigestive myoelectric complex (IDMEC), which appeared to occur in the antrum as well. The episode of intense spike activity was described as one of four cyclically recurring phases in the interdigestive state. Phase I is the phase of complete or almost complete absence of spike activity, phase III is the activity front. The phases II and IV are transition phases.
The duration of one cycle of the IDMEC was 90 to 114 minutes, and the propagation time (from stomach to terminal ileum) was 105 to 134 minutes. In the stomach, phase III lasted 12 ± 1.1 minutes, which was about twice as long as in the small intestine.
In all 109 interdigestive complexes studied by Code and Marlett, stomach and duodenum passed through the four phases almost synchroneously.

The motor correlate of the IDMEC has extensively been described by Itoh and co-workers (Itoh et al., 1977; Itoh et al., 1978a, 1978b). The myoelectric phases I to IV appear to correspond to phases in the interdigestive motor activity (phase of motor quiescence, phase of weak, 'irregular' contractions, phase of strong contractions and phase of subsiding contractions, respectively). In the antrum the phase of strong contractions is described as consisting of *grouped* strong contractions; groups of two to four strong contractions being alternated by short periods with weak or absent contractions. This description is in contradiction with the description of phase III given by Code and Marlett (1975) which says that in this phase almost every initial potential is followed by intense 'action potential' activity.
In the orad corpus, phase III is characterized by the occurrence of rhythmic tonic contractions, which look like the evelope of the phasic antral contractions (Fig.16).

In one of the figures of Itoh et al. (1978b) an interdigestive motor complex is shown that starts in the jejunum and is absent in the stomach, but the description in the text only speaks of complexes starting simultaneously in stomach and duodenum.
Finally it should be mentioned that Itoh and co-workers also reported the occurrence of interdigestive motor complexes in the lower esophageal sphincter (LES) (Itoh et al., 1978a). The LES-complexes are synchronous with the complexes in stomach and duodenum.

Interdigestive migrating complexes (IMC) have also been demonstrated in man, both electrically (with intraluminal electrodes (Fleckenstein, 1978) and with serosal electrodes (Stoddard et al., 1977)), and motorically (by means of intraluminal pressure measurements (a.o. Vantrappen et al., 1977a, 1977b).

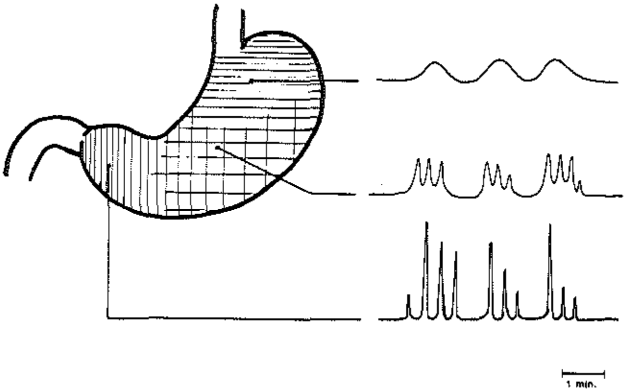

Fig.16 Contractile behaviour of the stomach during phase III (schematic). The proximal part of the corpus is only capable of performing tonic contractions, which form the envelope of the phasic antral contractions. In the distal part of the corpus a combination of phasic and tonic contractile activities is seen. After Itoh et al., 1977.

The numerous investigations into the mechanisms underlying the IMC will not be summarized here. It is only mentioned that an intact vagus nerve probably is not required for initiation and propagation of the complexes (Marik and Code, 1975; Weisbrodt et al., 1975; Ormsbee and Mir, 1977; Catchpole and Duthie, 1977; Mroz and Kelly, 1977; Thomas et al., 1979; Reverdin et al., 1979; Diamant et al., 1979), and furthermore, that the gastrointestinal hormone *motilin* probably plays an important role in the initiation of the complexes (Itoh et al., 1976; Wingate et al., 1976; Aizawa et al., 1977; Vantrappen et al., 1977a; Thomas et al., 1979; Lux et al., 1979; Itoh et al., 1979; Peeters et al., 1979).

4.2.5.2 Digestive pattern

Immediately after repletion of the stomach, the IMC is interrupted, not only in the stomach, but usually in the entire small intestine as well. The postprandial pattern which then sets in, is characterized by the presence of contractions of mediocre strength during almost 100% of the ECA cycles (Code and Marlett, 1975; Marik and Code, 1975; Ruckebusch and Bueno, 1975; Itoh et al., 1977; Ruckebusch and Bueno, 1977; de Wever et al., 1978; Eeckhout et al., 1978; Reverdin et al., 1979; Diamant et al., 1979).
The duration of the interruption (disruption) of the interdigestive pattern depends on the volume of the taken food and on its physicochemical composition (Ruckebusch and Bueno, 1976; de Wever et al., 1978). Disruptions of more than 20 hours duration have been reported (de Wever et al., 1978).
The interruption by food requires an intact vagus nerve (Marik and

Code, 1975; Weisbrodt et al., 1975; Reverdin et al., 1979; Diamant et al., 1979). Disruption of the IMC can also be accomplished by administration of gastrines (Weisbrodt et al., 1974; Marik and Code, 1975; Wingate et al., 1977).

4.2.6 Arrhythmias of gastric ECA

The rhythm of gastric Electrical Control Activity (ECA) in healthy conscious dogs is usually described as regular.
However, some reports on *arrhythmias* of gastric ECA can be found in the literature.
When acetylcholine is administered intra-arterially in the correct phase of the ECA cycle, a premature, *ectopic control potential* can be evoked (Daniel, 1965, 1966; Sarna et al., 1972b). These ectopic control potentials originate outside the normal gastric pacemaker area.
After intra-arterial administration of adrenergic substances a pattern consisting of a rapid succession of ectopic initial potentials without second potentials can be seen (Daniel, 1965, 1966). Since the same pattern can be produced by administration of atropine, Daniel called the pattern the 'sympathetic dominance pattern'.
Such episodes of fast ectopic (antral) activity occur spontaneously in conscious, fasting dogs (Bedi et al., 1972; Kelly and La Force, 1972; Code and Marlett, 1974). To denote the above-described rapid succession of ectopic initial potentials, Code and Marlett (1974) introduced the term *'tachygastria'*.
Recently, the occurrence of tachygastria in man has been described as well. Once it concerned a patient with gastric carcinoma (Hinder and Kelly, 1977), and twice it concerned patients with idiopathic gastric paresis (Telander et al., 1978; Sanders et al., 1979).
Several investigators reported the occurrence of ectopic ECA arrhythmias after *truncal vagotomy* (Nelsen et al., 1967; Kelly and Code, 1969; Wilbur and Kelly, 1973) and, less frequently, after *highly selective vagotomy* Stoddard et al., 1975; Rosenquist et al., 1977; Bortolotti et al., 1978). Part of these investigations were performed in the dog, part in man.
In some of the publications mentioned above, tachygastrias are present, either explicitly mentioned, or recognizable as such (Nelsen et al.,1967; Kelly and Code, 1969; Stoddard et al., 1975; Bortolotti et al., 1978).
The mechanism through which vagotomy leads to ectopic impulse formation is not yet known for certain. Sarna and Daniel (1974) supposed that elimination of the parasympathetic influence on the refractory properties of antral oscillators leads to 'unphase-locking' of those oscillators and thus to arrhythmias.

Nonectopic arrhythmias of gastric ECA, originating in the normal pacemaker area, have not yet been described in the literature.

4.3 Methods, materials and techniques used in our studies

Nine healthy dogs (Beagles) were used in our studies.
Extraluminal force transducers and electrodes (to be described below) were implanted under general anesthesia and using sterile operating technique.

The extraluminal strain-gauge force *transducers* used to record contractile activity were constructed as described by Bass and Wiley (1972) and calibrated by means of the method described by Schuurkes et al. (1977).

The construction of the bipolar (serosal) *electrodes* used, is shown in Fig.17.

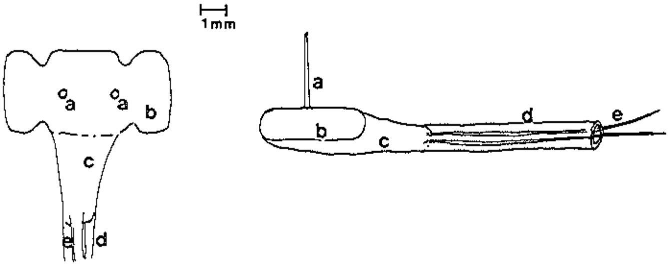

Fig.17 Construction of the bipolar serosal electrodes used in our studies.

a : electrodes proper
b : electrode base (polyvinylchloride)
c : epoxy resin
d : tubing
e : wires

The material used for our electrodes was silver/silver-chloride. Two pointed electrodes with a base diameter of 0.2 mm and a length of 3 mm were mounted, 2 mm apart, in the electrode base. The latter was provided with four notches to facilitate its attachment to the serosal surface of the stomach.
To each of the electrodes proper a teflon-coated stainless steel wire with a diameter of 0.25 mm was attached (Bio-med Wire©, Cooner Company Inc., California, U.S.A.). The two wires together were enveloped by a silicone rubber tubing (Silastic©, Dow Corning, Michigan, U.S.A.) with an inner diameter of 0.68 mm, outer diameter 1.18 mm.
We found it to be of outmost importance that the stainless steel wires were kept freely movable in the tubing. When the tubing was filled up with silicone rubber, the wires turned out to break soon. The same applied to the combination of the individual electrode leads to one, rather rigid, cable.

The positions of electrodes and force transducers which were standard in our studies are illustrated in Fig.18.

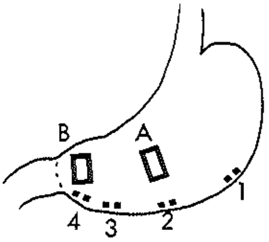

Fig.18 Standard positions of electrodes (1 - 4) and force transducers (A and B).

All electrodes were placed in a longitudinal direction, along the greater curvature. The distances of the electrodes 1 - 4 to the pyloric sphincter

were 12, 7, 4 and 2 cm.
The position of electrode 1 was chosen for the fact that in previous experiments it appeared to be the most proximal site from which a stable ECA could always be derived. This observation is in accordance with those made by others (Kelly et al., 1969; Sarna et al., 1972a).
Occasionally, additional electrodes were implanted, e.g. on the duodenum.
For monopolar recording a disposable Ag/AgCl ECG-electrode (Hewlett Packard 14245A) was placed on the lateral side of the right hind leg.

The extraluminal force transducers were not used in all studies. When used, they were placed in a transverse direction. Transducer A was placed at the level of electrode 2, transducer B at the level of electrode 4.
The following methods of *signal transmission* were used:

1. using an electrical connector protruding from the skin, enabling cable contact at each recording session;
2. direct transit of the lead wires through the skin, provided with an extracorporal connector and protected with a canvas jacket;
3. radiotelemetric transmission with the aid of an implanted 6-channel transmitter, described by Besseling et al. (1976).

Recordings were made with conscious dogs, both fasting and postprandially. During the recording sessions, lasting from 1 to 16 hours, the dogs lay unrestrained in a cage similar to their normal housing.

From all dogs *bipolar* signals (potential differences between the electrodes proper of each bipolar electrode) were obtained.
From five dogs *monopolar* signals (potential differences between serosal and reference electrodes) were recorded as well. Monopolar recordings were made in order to obtain a better insight into the genesis of the gastroelectromyographic signal (as will be discussed later on).

For filtering and amplification of the gastroelectromyographic signals Van Gogh EP-8b 8-channel polygraphes were used.
The signals were filtered with first-order RC-filters (attenuation 6 dB/oct). In *monopolar* recording the cutoff-frequencies of high-pass and low-pass filters were 0.012⊗) and 35 Hz, respectively.
In our standard *bipolar* recording technique these frequencies were 0.5⊗⊗) and 15 Hz.
All signals were recorded on chart (curvilinearly) as well as on magnetic tape, using a 14-channel recorder (Racal Store-14), with a tape speed of 15/16 inch per second.
Connections were such that in the monopolar recordings an upward deflection indicates positivity of the exploring electrode with respect to the indifferent electrode on the right hind leg.
In the bipolar recordings an upward deflection indicates that the orad electrode is positive with respect to the caudad one.

4.4 Configuration of serosal gastroelectromyographic signals in the dog

4.4.1 Results

⊗) A cutoff-frequency of 0.012 Hz corresponds to a time constant (τ) of 14 s.

⊗⊗) A cutoff-frequency of 0.5 Hz corresponds to a time constant (τ) of 0.3 s.

4.4.1.1 Configuration of monopolarly recorded signals

Fig.19 gives an example of the signals recorded from the *mechanically inactive* stomach of the conscious dog.

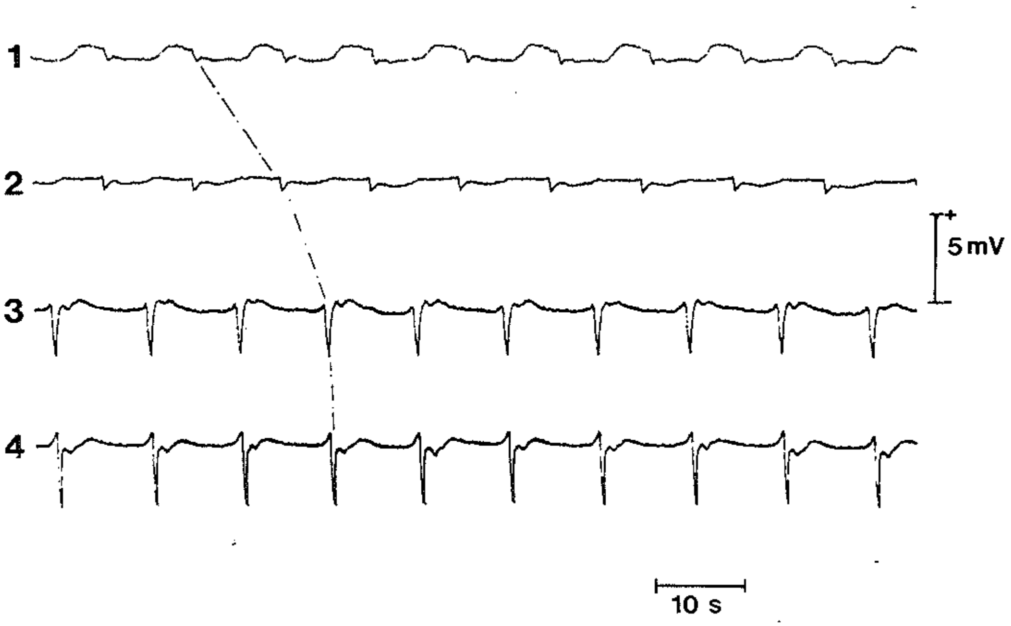

Fig.19 Monopolarly recorded serosal signals. Filter settings: high-pass 0.012 Hz, low-pass 35 Hz. Fasting, conscious dog. Motor quiescence. For positions of electrodes see Fig.18. The configuration of the signal obtained from electrode 4 is somewhat atypical.

The signals obtained from electrode 1 (12 cm from the pylorus) had a configuration which can be described as close to sinusoidal. Often the signals obtained from electrode 2 (7 cm from the pylorus) had a similar appearance. The initial potentials are the relatively fast, mainly negative, deflections. Sometimes the recognition of the initial potentials in the monopolar signals from the electrodes 1 and 2 was hardly possible.

At the level of electrodes 3 and 4 (4 and 2 cm from the pylorus), however, the monopolar signals obtained during motor quiescence were dominated by the regularly recurring initial potentials. This as a consequence of a higher amplitude of the initial potential and a lower amplitude of potential changes between the initial potentials.

Although the amplitude of the initial potentials varied even intraindividually, it was always higher in the antrum than in the corpus.

At all gastric levels the negative deflection of the initial potential was preceded by a positive deflection. The amplitude of this deflection increased towards the pylorus. At the level of electrode 4 the typical configuration of the monopolarly recorded initial potential was biphasic, consisting of a positive deflection and a negative deflection of approximately equal amplitude (Fig.20).

Fig.20 Typical biphasic configuration of initial potentials recorded monopolarly from electrode 4.
Motor quiescence. Filter settings as described.

Although this cannot be concluded from Fig.19, it became clear from many other, less regular, recordings, that the initial potentials were propagated from corpus to pylorus as indicated by the broken line in Fig.19. The initial potentials arrived at electrode 4 12 to 15 seconds after passing electrode 1.
The propagation velocity of the initial potentials was much greater in the antrum than in the corpus, but the propagation velocities were not studied in detail.

When phasic contractions occurred, two types of changes in the monopolar signals were observed (Fig.21). These changes were most consistent in the antrum.

The first type consisted of a slow, more or less biphasic (negative-positive) deflection; the *second potential.*

The second type consisted of rapid oscillations (frequency usually about 3 to 4 Hz); the *spikes.*

The second potentials followed the initial potentials by 4 to 6.5 seconds. The *interpotential segment* (the signal segment between the initial and second potential) was always below the isoelectric level.
The summits of the phasic contractions always preceded the ends of the second potentials; usually the contraction summit coincided with the negative deflection of the second potential.

Whereas second potentials without spikes were observed frequently, *spikes without second potentials were never seen.*

The spikes, when present, preceded the biphasic second potential. They followed the initial potential by 2 to 5 seconds. Maximum spike activity preceded the summit of the contractions.
Spikes predominantly occurred in the terminal antrum, but were observed in recordings from other gastric levels as well. Neither in the corpus, nor in the antrum, spiking appeared to be a necessary condition for the occurrence of phasic contractile activity.

Fig.22 illustrates the effect of *high-pass filtering* on initial potential, interpotential segment, spikes and second potential.

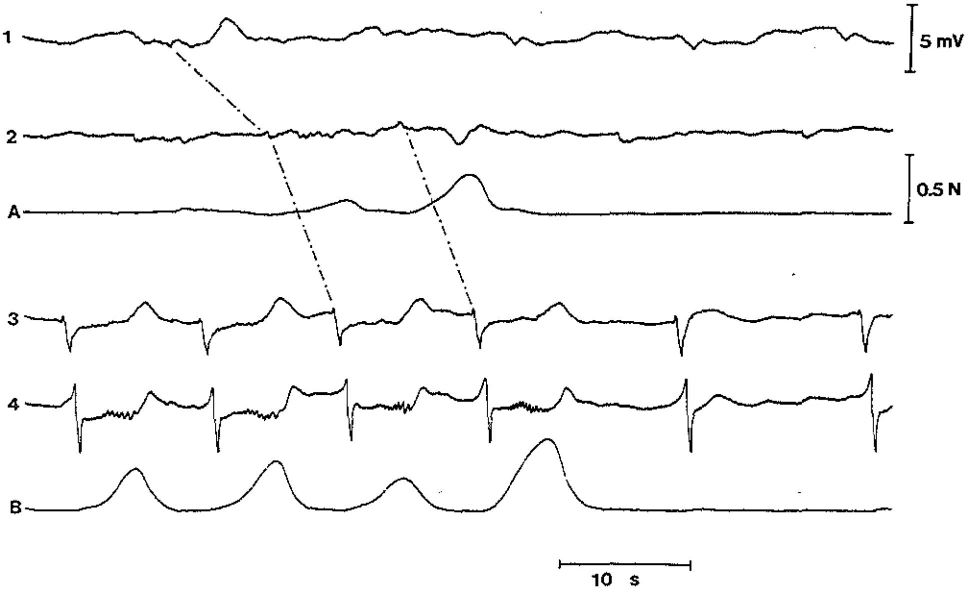

Fig.21 *The two types of contraction-related changes in the monopolarly recorded signals: spikes and second potentials.*
In this example the spikes are present almost exclusively in the antrum. For positions of electrodes (1 - 4) and transducers (A and B) see Fig.18.

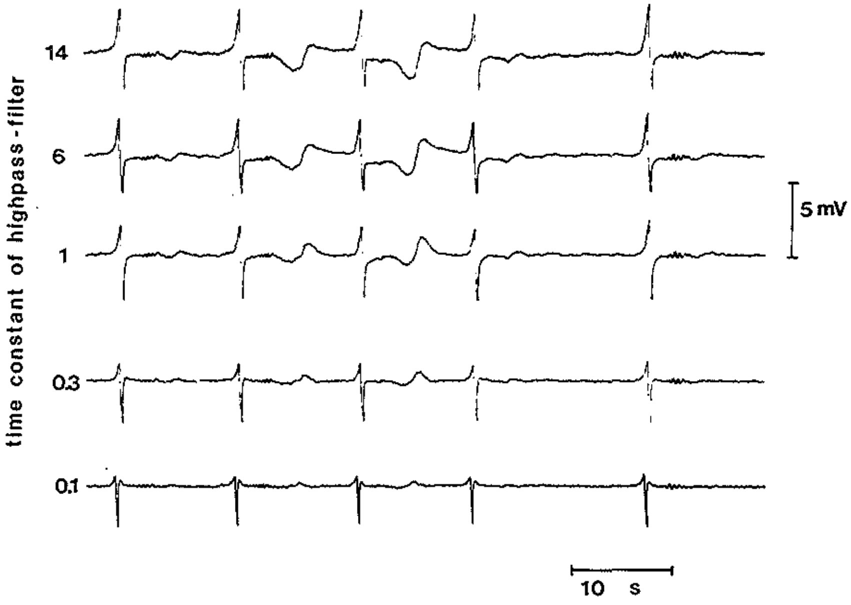

Fig.22 *The effects of high-pass filtering on the configuration of the monopolar signal obtained from electrode 4. The frequently used time constants 6, 1, 0.3 and 0.1 (s) correspond to cutoff-frequencies at 0.27 Hz, 0.16 Hz, 0.53 Hz and 1.6 Hz.*

When time constants of 1 second and shorter are used, the positive deflection of the initial potential and the negative deflection of the second potential become smaller and, as could be expected, the interpotential segment becomes isoelectric.

4.4.1.2 Configuration of bipolarly recorded signals.

The configuration of the *initial potentials* recorded with our standard bipolar technique (interelectrode distance 2 mm, bandwidth 0.5 - 15 Hz) was always biphasic, i.e. *negative-positive*. This configuration can be understood by realizing that the bipolarly recorded signal can be regarded as the difference between two monopolar signals (Fig.23).

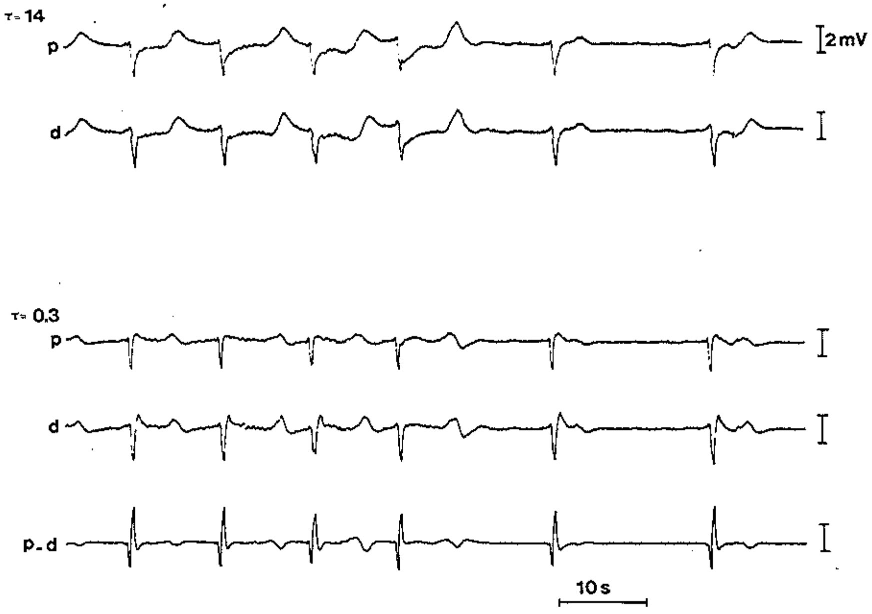

Fig. 23 Monopolar signals recorded from the proximal (p) and distal (d) electrodes of bipolar electrode 3, and the differential signal p - d, which is the bipolar signal recorded with our standard technique.

The *second potentials* in the bipolarly recorded signals were always smaller than in the corresponding monopolar signals. The configuration of the bipolarly recorded second potentials was somewhat variable; a biphasic, positive-negative configuration was seen most frequently, however.
In our bipolar signals depressions or elevations of the *interpotential segments* were not observed; the signals recorded bipolarly from electrodes 1 and 2 were far from sinusoidal.
The amplitudes of the *spikes* in the bipolar signals were smaller than in the monopolar signals. Due to a reduced amount of noise

in the bipolarly recorded signals, spikes could sometimes be recognized better from the bipolar than from the monopolar signals, however.

For use in conscious animals, the bipolar technique appeared to be more practical than the monopolar. With a bipolar technique most of the movement artifacts, electrocardiographic signals and 50 or 60 Hz-interference was suppressed. Recording from freely moving animals appeared to be much easier with the bipolar than with the monopolar technique.

In three of our (nine) dogs a reversed polarity of the initial potentials recorded bipolarly from electrode 4 was frequently observed. The retrograde conduction of initial potentials, indicated by this sign, was confirmed by studying the corresponding monopolar signals (Fig.24).

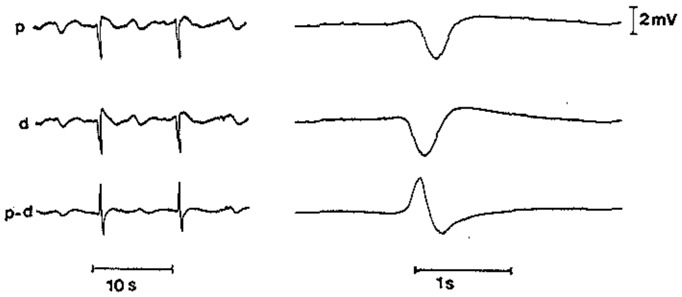

Fig.24 Retrograde conduction of initial potentials at the level of electrode 4, as observed in three dogs.

Left : usual time scale.
Right: expanded time scale.

p = monopolar signal recorded from proximal electrode.
d = monopolar signal recorded from distal electrode.
p-d = bipolar signal.

It had to be concluded that in these cases the muscle underneath electrode 4 was activated in retrograde direction (whereas the rest of the stomach was activated aborally).

4.4.1.3 Relations between phasic contractile force and the configuration of the monopolar signal

At visual examination, relations appeared to exist between the amplitude of the second potential and the force of the corresponding phasic contraction, as well as between the duration of the interpotential segment and contractile force (Fig.25).

These relations were not studied in detail, but the amplitudes of the second potentials, the durations of the interpotential segments and the amplitudes of the phasic contractions in a random series of 80 consecutive ECA cycles were measured (with a ruler).

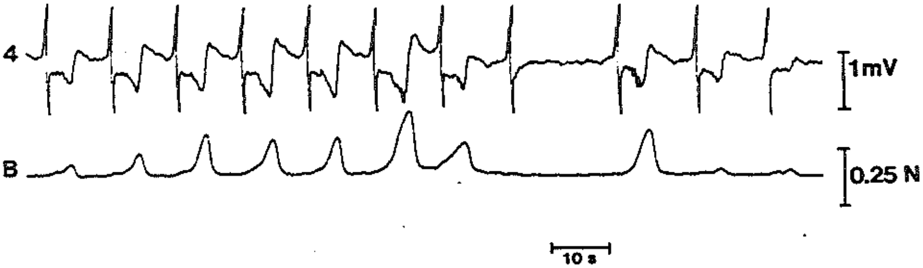

Fig.25 Monopolar signal recorded from electrode 4 (0.012 - 35 Hz) and the corresponding contractile signal, recorded with transducer B. Fasting dog.

The smallest contraction measurable with our working-method was about 0.01 N; as a consequence, contractions smaller than 0.01 N were booked as absence of contractile activity (contractile force 0). When the second potential was absent, second potential amplitude and interpotential segment duration were booked as 0.

As indicated by Fig.26, stronger phasic contractions were accompanied with larger second potentials. It appeared to be impossible, however, to discriminate for certain between absence and presence of phasic contractile activity on the basis of the amplitude of the second potential. Furthermore, some rather strong contractions (e.g. those marked as a, b and c in Fig.26) were accompanied with relatively small second potentials.

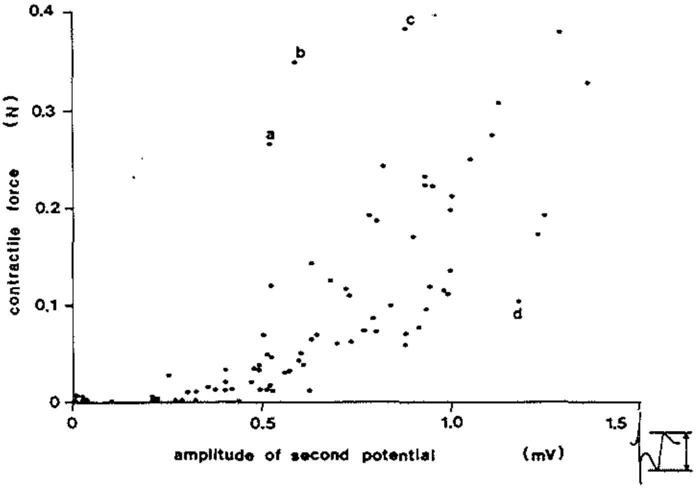

Fig.26 Relation between amplitude of second potential and contractile force. 80 consecutive ECA cycles. Electrode 4, transducer B. Amplitudes of second potential and contractile force measured with a ruler. Fasting dog. Four rather excentric points were marked as a, b, c and d.

The longer the duration of the interpotential segment was, the greater the contractile force appeared to be. The shortest interpotential segment observed had a duration of 4 seconds (Fig.27).

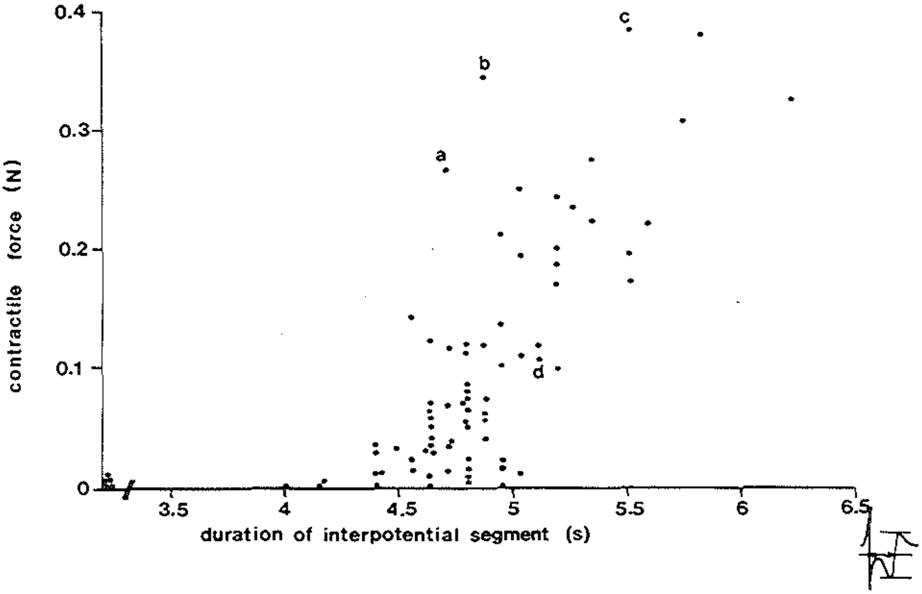

Fig.27 Relation between duration of the interpotential segment and contractile force. Same ECA cycles as in Fig.26. Points a, b, c and d correspond to points a, b, c and d in Fig.26.

As could be expected from Figs.26 and 27, the amplitude of the second potential and the duration of the interpotential segment appeared to be related as well (Fig.28). Although the presented data are limited, this latter relation seems to be stronger than the relations between contractile force on the one hand and second potential amplitude and interpotential segment duration on the other hand. The points a, b, c and d, excentric in Figs. 26 and 27, merge into the cloud of points in Fig.28.

When second potential amplitude, duration of the interpotential segment and contractile force are plotted as a function of ECA interval number, it appears that the parameters of the second potential might be used to monitor motor patterns as a function of time, when only myoelectrical activity is available (Fig.29).

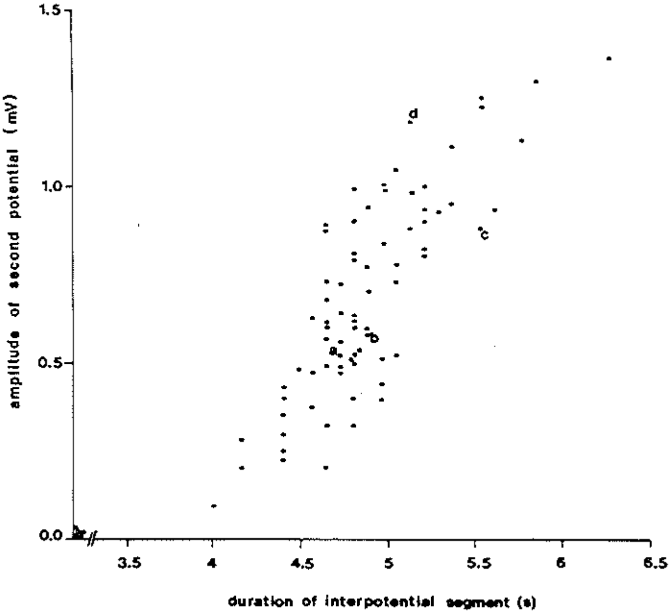

Fig.28 *Relation between duration of interpotential segment and amplitude of the second potential. Same 80 ECA cycles as in Figs. 26 and 27. Points a, b, c and d correspond to the points identically marked in Figs. 26 and 27.*

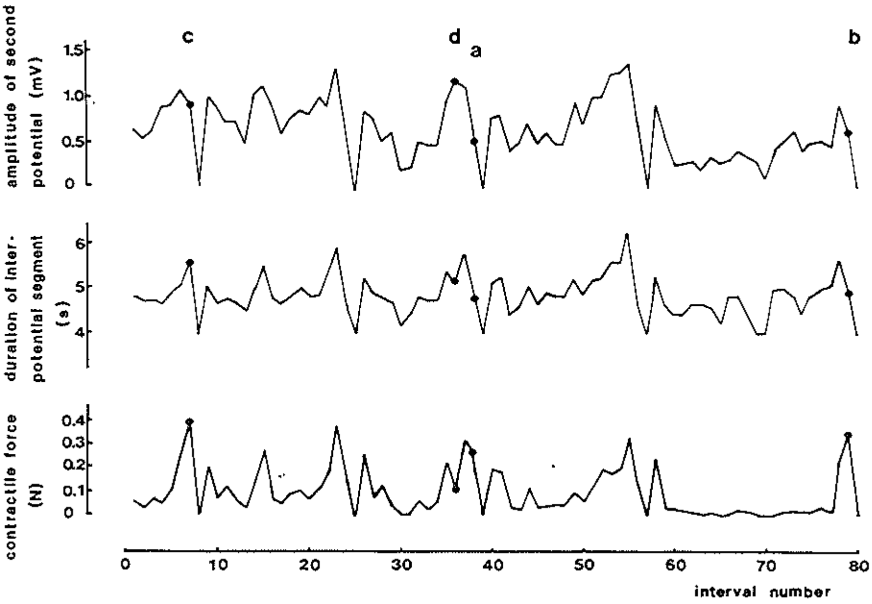

Fig.29 *Phasic contractile force, duration of interpotential segment and amplitude of second potential versus ECA interval number. Same 80 ECA intervals as in Figs. 26-28. Points a, b, c and d as in Figs. 26-28. (For clearness' sake all points of each trace were connected.)*

4.4.1.4 *Relations between phasic contractile force and the configuration of the bipolar signal: the 'ERA score'*

In order to assess phasic contractile activity on the basis of the bipolar signals recorded with our standard recording technique, an *'ERA score'* was introduced.
Based on data presented in previous chapters, ERA was scored *higher* as:
a) the duration of the interpotential segment,
b) the amplitude of the second potential,
c) the amplitude of the spikes (when present), and
d) the duration of the spike burst *increased*.

When no ERA was present, the score was 0. The maximum ERA that occurred at a specific electrode was scored as 3.
In the bipolar signals obtained from electrode 1 often each initial potential was followed by a second potential, even during motor quiescence. Therefore, in the signals from electrode 1, small second potentials (with short interpotential segments) were scored as 0.
Because of the interindividual and intra-individual variabilities, our ERA score cannot be used for comparison of scores in different dogs and different electrode positions.

In a series of 331 consecutive ECA cycles, the attached ERA scores were compared with the actually measured contraction amplitudes. This was done both for (bipolar) signals recorded from electrode 2 (compared with signals from transducer A) and for signals recorded from electrode 4 (compared with signals from transducer B). The results are displayed graphically in Figs.30 and 31, respectively.

As could have been expected, some overlap between the four categories appeared to be present. Nevertheless, higher ERA scores were related with stronger contractions and the classification into four categories appeared to be a defensible one.

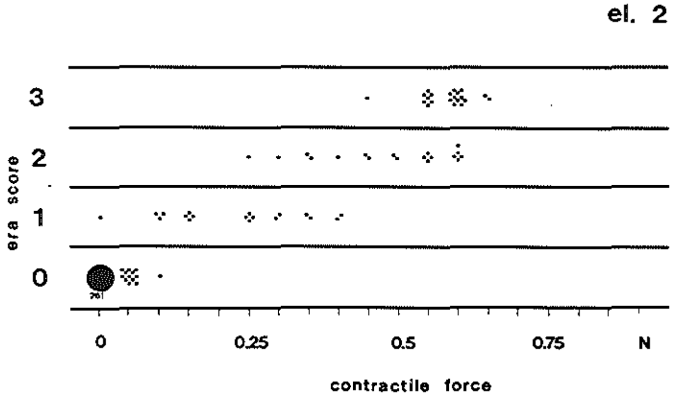

Fig.30 Relation between ERA score attached and contractile force measured in a series of 331 consecutive ECA intervals. Electrode 2, transducer A.

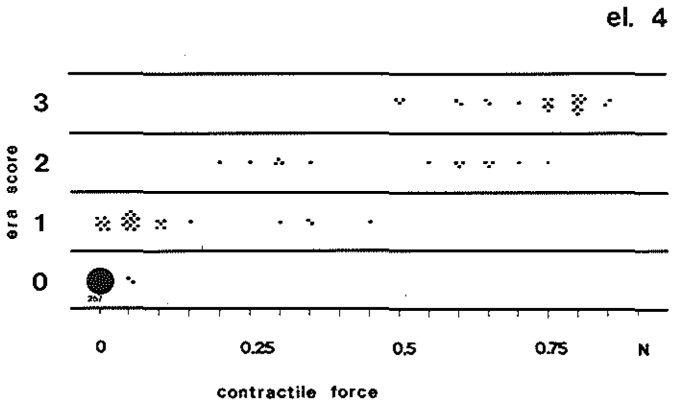

Fig.31 Relation between ERA score and contractile force recorded from electrode 4 and transducer B. Same 331 ECA intervals as in Fig.30.

As illustrated in Fig.32, the ERA score appeared to provide a means of monitoring gastric motor patterns as a function of time.

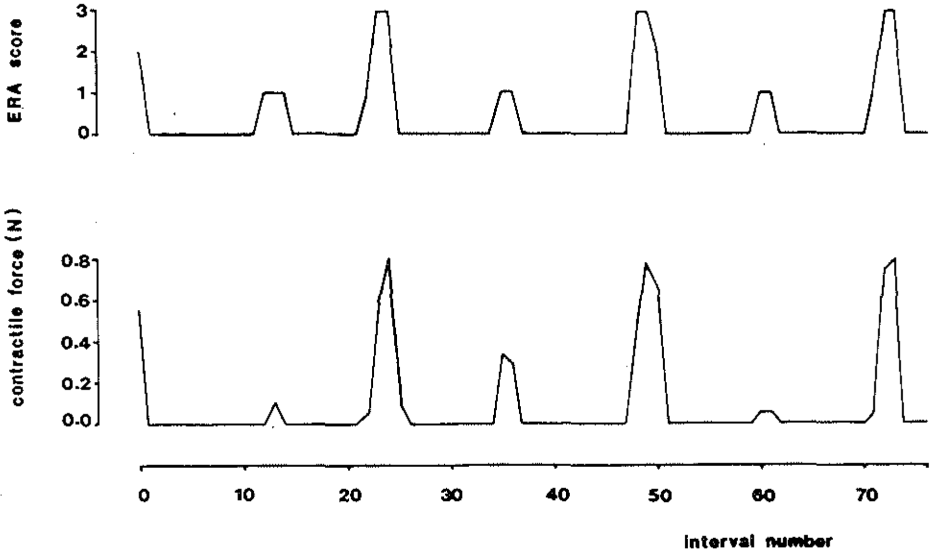

Fig.32 ERA score (electrode 4) and contractile force (transducer B) versus ECA interval number. 77 consecutive ECA intervals, taken from the 331 intervals of Figs.30 and 31. (For clearness' sake all points of each trace were connected.)

4.4.2 Discussion

4.4.2.1 Configuration of monopolarly recorded signals

In the literature the monopolarly recorded *initial potentials* are almost invariably described as *triphasic* (positive-negative-positive). In our opinion the configuration of the initial potential is rather *biphasic* (positive-negative) than triphasic.

This discrepancy is probably due to the use of different time constants. Whereas most investigators used high-pass filters with time constants of 1 second and shorter, we used a time constant of 14 seconds.

From a theoretical point of view, it can be considered a serious mistake to utilize a high-pass filter with a cutoff-frequency higher than the repetition frequency of the signal to be described. In the case of the myoelectrical activity of the canine stomach, the repetition frequency is about 5 cpm or 0.085 Hz. Since a time constant of 1 s corresponds to a cutoff-frequency of 0.16 Hz, a high-pass filter with a time constant of 1 s does not transfer the fundamental gastric frequency and, in consequence, distorts the gastroelectromyographic signal. As demonstrated in our study, distortion of the initial potential indeed takes place when time constants of 1 s and shorter are used. The positive deflection becomes smaller with decreasing time constants and there may even arise a secondary positive deflection following the negative deflection (Fig.22).

Although it can be defensible to use smaller time constants, it should be avoided to refer to the configuration of the signal thus obtained as 'the typical configuration of the monopolar signal'. Likewise, distortion of *interpotential segment* and *second potential* occurs when time constants of 1 s or shorter are used in monopolar recording. As a consequence, the segments of the corporal monopolar signals in between the initial potentials have been described as isoelectric. In reality, these portions of the corporal signals exhibit slow potential changes with amplitudes as high as those of the initial potentials. A sinusoidal configuration of myoelectric signals from the corpus has been described, however, by Nelsen et al. (1967).

The wide-spread use of (too) small time constants can also be considered responsible for the fact that the interpotential segment has not yet been described as such. Recorded with time constants of 1 s and shorter the interpotential segment is isoelectric (see Fig.22) and therefore of little interest.

In our studies, contraction-related *second potentials* without spikes were frequently observed, whereas spikes without second potential were never seen. In our opinion, the contraction-related second potential forms an essential part of the gastroelectromyographic signal, whether recorded monopolarly or bipolarly.

In the literature the misconception that phasic contractions of gastric smooth muscle only occur in relation with spikes, is frequently met. This misconception is probably due to three factors:

- by using lower time constants the second potentials are attenuated,
- in the small intestine spikes probably always precede the phasic contractions (Daniel et al., 1959; Bortoff, 1976), although some investigators (e.g. Grivel and Ruckebusch, 1972) claimed the existence of spike-free activation of intestinal smooth muscle, and
- spikes do occur in the stomach.

Richter (1924) described the relation between the monopolarly recorded second potential ('w-wave' in Richter's terminology) and phasic contractile activity in the anesthetized dog as follows: 'the slow phase w of the action currents coincides both in form and in amplitude very closely with the contraction of the circular coat of fibers'.

Regarding the possibility that the observed contraction-related potential changes are not a part of the myoelectric activity, but are movement artifacts, Richter stated: 'I have tried to reassure myself on this point by pulling on the electrodes and then noting the electrical changes. It is only with severe pulling that any changes appear and these are relatively small'.

In the early publications by Daniel and colleagues (Daniel, 1965, 1966; Daniel and Irwin, 1968) and in one of the early publications by the Mayo group (Code et al., 1968) justice was also done to the second potential. At the same time Papasova et al. (1968) wrote: 'the second component (= second potential) is correlated with contraction and contractions tend to be larger when spikes are superimposed on the second slow wave, but the spikes are apparently not necessary for contraction, hence the second potential does not represent fused spikes'.

In most later studies, however, including those by Daniel and Sarna (Sarna et al., 1972a, 1972b, 1972c; Sarna and Daniel, 1973,1976) and those by the group at the Mayo Clinic (Kelly et al., 1968,1969; Kelly and Code, 1969, 1971; Kelly and La Force, 1972; Code and Marlett, 1974, 1975) the second potential is, at best, regarded as a companion of spikes or as fused spikes. As stated earlier, in the terminology used by Sarna and Daniel, ERA is a synonym for fast activity, spike activity or action potentials, while the second potential is left unnamed and undiscussed.

According to the *core-conductor or cable theory,* the monopolarly recorded extracellular signal approximates the *second time derivative* of the intracellularly recorded signal (Plonsey, 1969; Geddes, 1972; Bortoff, 1975a). The second derivatives of synthesized signals resembling those recorded intracellularly from gastric smooth muscle indeed show much resemblance to monopolarly recorded gastroelectromyographic signals (Fig.33).

Obviously, the positive-negative initial potential is the extracellular manifestation of the depolarization. The gradual repolarization in the left part of Fig.33 does not come to light in the extracellular signal, whereas the steeper repolarization in the right part of the figure gives rise to a small, negative-positive second potential.

Larger second potentials and depressions of the interpotential segment cannot be understood with the aid of the cable theory. Likewise, the configurations of the 'sinusoidal' monopolar signals that are recorded from the corpus cannot be understood as second derivatives of intracellular signals.

Looking at monopolarly recorded gastroelectromyographic signals, particularly those recorded from the corpus, one gets the impression that they contain a component resembling the *inverted intracellular signal* (Fig.34).

In the antral signals, the presence of an (attenuated) inverted version of the intracellular signal would account for the depression of the interpotential segment and the large second potentials present in these signals (Fig.35).

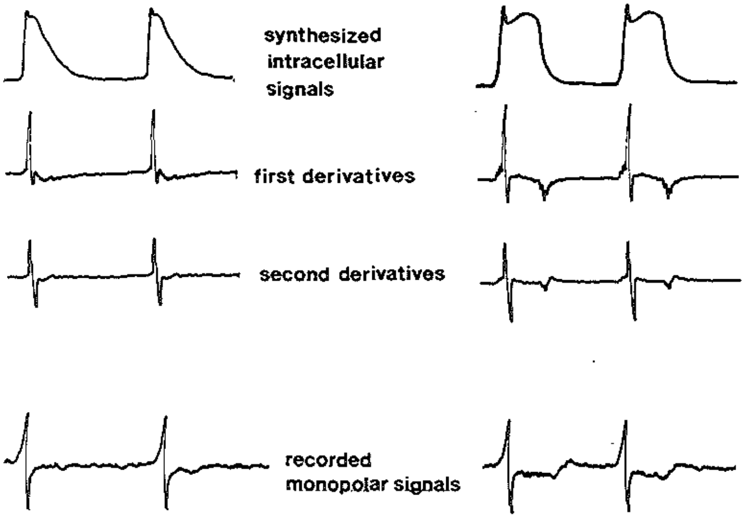

Fig.33 Resemblance of the second derivatives of intracellular wave forms to gastroelectromyographic signals recorded monopolarly from the antrum. The left part of the Figure shows the configurations in the absence of a plateau in the intracellular signal, in the right part a plateau is present. The intracellular signals were synthesized with an Exact 202 Wave Form Synthesizer. Differentiations were accomplished electronically. The bottom trace shows signals recorded monopolarly from electrode 4.

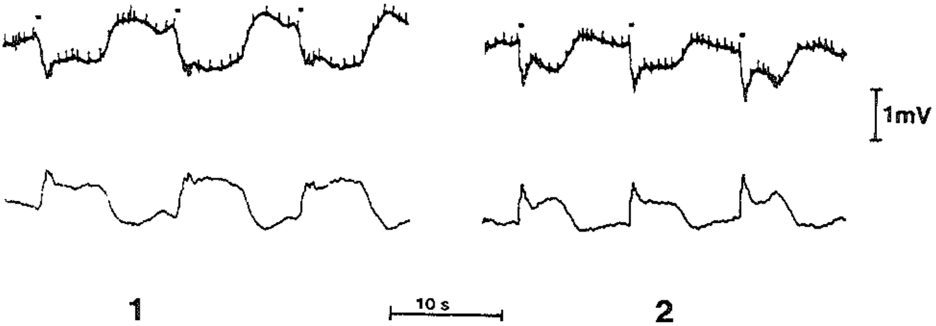

Fig.34 Signals, recorded monopolarly from the corpus (electrodes 1 and 2).

Upper signals: original signals, as recorded on tape (0.012 - 35 Hz).
Lower signals: the same signals after inversion and low-pass filtering (f = 6 Hz)

The initial potentials are indicated with dots.
Note the resemblance of the inverted signals with the intracellular signals described in Chapter 3.3.

We conclude that the monopolar serosal signal can be understood by assuming that it consists of two components:

a) a component that can be understood with the aid of the cable theory, and

b) a component resembling the inverted intracellular signal.

In the corpus component b) is predominant, in the antrum component a) predominates.

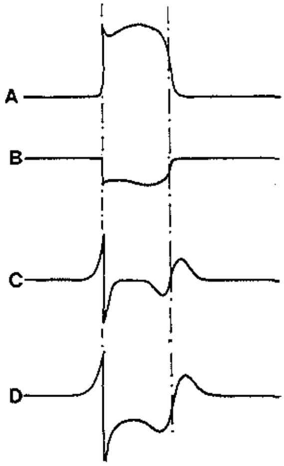

Fig.35 Construction of a monopolar antral signal containing an inverted intracellular component (schematic).

A : intracellular waveform
B : inverted (and attenuated) intracellular signal
C : field potential (second derivative of intracellular waveform)
D : sum of B and C.

4.4.2.2 Configuration of bipolarly recorded signals

As stated before, the bipolar signal recorded with our (conventional) electrodes can best be regarded as the difference between two monopolar signals.

According to cable theory, however, the bipolarly recorded signal should resemble the first derivative of the intracellular signal (Bortoff, 1975a). The theory only holds, however, when all extracellular longitudinal current flows through a very thin layer of extracellular fluid and the electrodes are very closely spaced. In 1945, Bozler recorded bipolarly from the canine stomach and predicted the intracellular waveform by integrating the obtained signal graphically. He used a specially constructed bipolar electrode with an interelectrode distance of only 0.6 mm (Bozler, 1945). The bipolar signals recorded with conventional electrodes like ours do *not* resemble the first derivative of the intracellular waveform; in attempts to understand the configuration of our bipolar signals, reference to the cable model is fruitless.

4.4.2.3 Relations between phasic contractile force and the configuration of the monopolar signal

The already cited work of Richter points at the existence of a relation between the amplitude of the second potential and the contractile force exerted by the muscle (Richter, 1924).
To our knowledge other indications of the existence of such a relation are not available in the literature.
It is known from investigations into the intracellular electrical activity of gastric smooth muscle that contractile force increases with the amplitude of the plateau (see chapter 3.3). Since the amplitude of the plateau seems to be related to the rate of repolarization and thus to the amplitude of the second potential, the observed relation between amplitude of the second potential and amplitude of the phasic contraction is in accordance with the results of intracellular studies.
Our finding that the amplitude of the phasic contraction increases with increasing duration of the interpotential segment is in accordance with the observation that contractile force increases with increasing duration of the plateau of the intracellularly recorded action potential (see Fig.9).
These findings again stress the physiological relevance of the second potential, a signal component that has been treated in a stepmotherly fashion in the literature.

4.4.2.4 Relations between phasic contractile force and the configuration of the bipolar signal: the 'ERA score'

To our knowledge, an ERA score had never been described in the literature. A generally accepted classification however, is the classification into present and absent ERA. Such a classification was used e.g. by Code and Marlett (1975).
In our experience, the distinction between absent and present contractile activity (made on the basis of the myoelectrical signal) is just as difficult as the distinction between weak, strong and very strong contractions. The use of an ERA score is, of course, not equivalent to the use of (extraluminal) force transducers. The ERA score merely provides a tool for the extraction of information from the myoelectrical signal.

4.5 Ectopic ECA arrhythmias in the canine stomach

4.5.1 Results

4.5.1.1 Ectopic Control Potentials (ECP's)

Most ECP's were observed in the first week after implantation of the electrodes. After the first week ECP's were only occasionally present. Most, but not all, ECP's occurred during episodes of motor quiescence, either during phase I of the IMC, or during short-lived episodes of motor quiescence in the absence of an IMC.

In one of the dogs an ECP occurred in the postprandial phase each time the animal drank (cold) water.

Single as well as *repetitive* ECP's (ECP's in salvo) were observed. Single ECP's could be divided into:

- *interpolated ECP's*, which do not interfere with the generation and conduction of the nonectopic control potentials (NECP's), and
- *ECP's with compensatory pause.* The compensatory pause is the consequence of a blocked conduction of the next NECP, caused by the refractory period which follows the ECP.

These three types of ECP's (single interpolated, single with compensatory pause and repetitive) are illustrated in Fig.36.

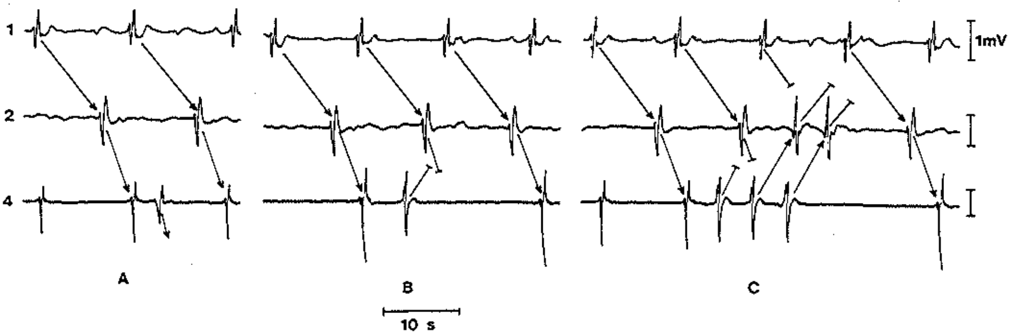

Fig.36 A. *Single, interpolated ECP, not interfering with the nonectopic rhythm. The ECP passes electrode 4 in antegrade direction (indicated by the normal polarity of the initial potential); its origin must be between electrodes 2 and 4.*

B. *Single ECP with compansatory pause. The ECP passes electrode 4 in retrograde direction (reversed polarity); its origin must be distal to electrode 4. The conduction of the next NECP is blocked, but the third NECP is propagated again in a normal fashion. As a consequence, the duration of the compensatory pause is equal to twice the duration of the normal ECA interval minus the duration of the interval between the ECP and the NECP preceding it.*

C. *Repetitive ECP's (salvo of three ECP's). The ECP's arise distal to electrode 4. In its retrograde propagation the first ECP collides with a NECP before reaching electrode 2. The last two ECP's reach electrode 2. There is a compensatory pause.*

It was noticed that the configurations of the ECP's differed from those of the NECP's at the same level by being broader. In addition, the *monopolarly* recorded ECP's had a reduced positive deflection (Fig.37).

In a random sample of 100 ECP's out of the material from our nine dogs, the following distribution of the sites of origin of ECP's was found:

origin between electrodes 1 and 2 (7 - 12 cm from pylorus) : 8
origin between electrodes 2 and 3 (4 - 7 cm from pylorus) : 12
origin between electrodes 3 and 4 (2 - 4 cm from pylorus) : 25
origin distal to electrode 4 (0 - 2 cm from pylorus) : 55
100

It seems that the inclination towards ectopic impulse formation increases in the direction of the pylorus.

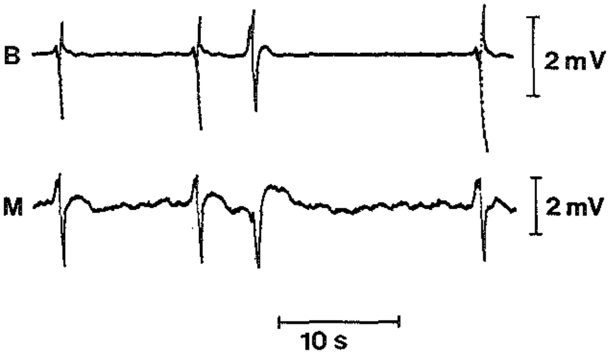

Fig.37 *Configuration of ECP and NECP's in signals recorded bipolarly (B) and monopolarly (M) from electrode 4.*

Finally the occurrence of an interesting type of arrhythmia has to be mentioned. This arrhythmia consisted of an apparently normal initial potential followed after a very short time (2 seconds or less) by an extra potential (Fig.38).

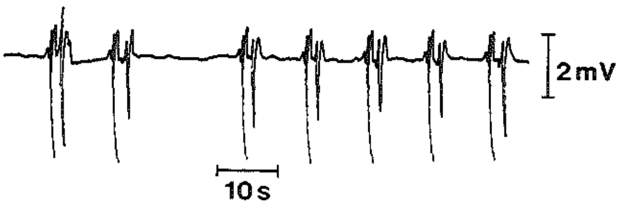

Fig.38 *Arrhythmia, recorded bipolarly from electrode 4. The extra potentials were observed only in the signal from electrode 4 and were not propagated noticeably.*

In the form shown in Fig.38 this type of arrhythmia only occurred in three of our dogs, always in the first week after implantation.

4.5.1.2 Tachygastrias

In 5 of our 9 dogs tachygastrias[⊠] were observed. Most tachygastrias occurred in the first week after implantation of the electrodes. Only in 3 of the dogs spontaneous tachygastrias occurred after the second week after implantation. On an average, the postoperative tachygastrias were of longer duration that the tachygastrias occurring after recovery.

Most characteristics of the observed tachygastrias can be described on the basis of Fig.39.

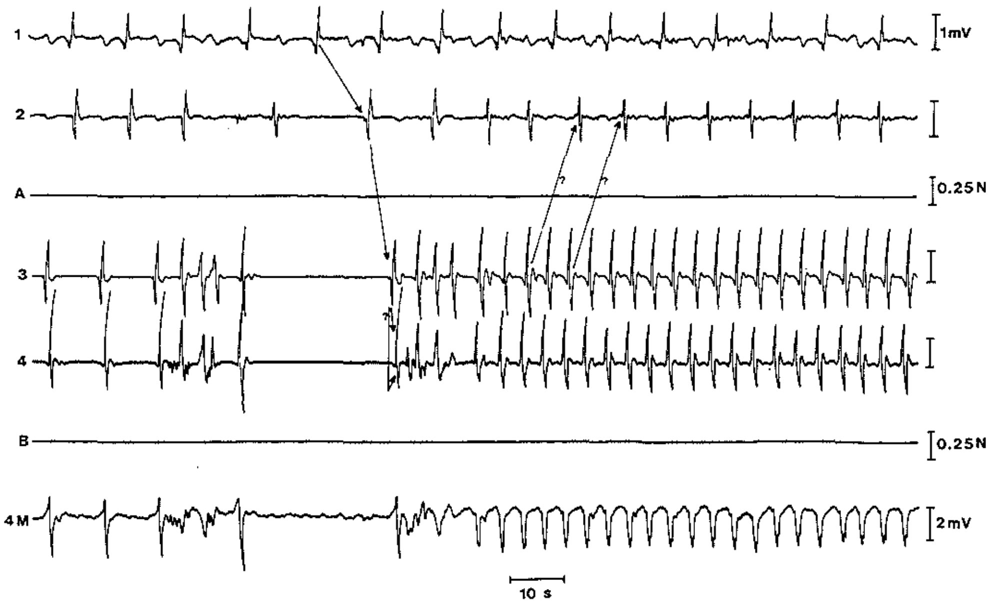

Fig.39 Regular tachygastria.
4M is the signal recorded monopolarly from electrode 4.
1, 2, 3 and 4 are bipolar signals.

In the left part of Fig.39, a number of ECP's followed by a compensatory pause can be seen. After that, a tachygastria ensues which begins as an irregular tachygastria and continues as a regular tachygastria. Such an irregular beginning of a regular tachygastria was observed frequently.

In Fig.39 the mean duration of the interval between successive tachygastric potentials is 4.05 seconds, corresponding to a repetition frequency of 14.8 cpm.

[⊠] We define tachygastrias as rapid successions of ECP's, lasting for more than 1 minute.

In the signals recorded monopolarly from electrode 4 the positive deflection is absent or almost absent, as was already described for ECP's. The figure further shows the often observed retrograde conduction of every second tachygastric potential (1 : 2 block). In this case such a block is present between electrode 3 and electrode 2. Retrograde activation at the level of electrode 2 is proven by the reversed polarity of the initial potentials and by their frequency. The two question marks at this level point only at the uncertainty about which initial potential at electrode 3 is related to which initial potential at electrode 2. The muscle under electrode 1 is not yet influenced by the tachygastria, but a few minutes later (not shown) the tachygastria will rule out the normal pacemaker in the corpus.

In this example it is difficult to establish the site of origin of the tachygastria because of the reversed polarities of the NECP's at electrode 4. When it is assumed that the NECP's pass electrode 4 in retrograde direction, the tachygastria shown here arises distal to electrode 4, otherwise the site of origin is between electrode 3 and 4. Finally, Fig.39 illustrates the observation that tachygastrias were always accompanied with motor quiescence. It could not be concluded whether tachygastrias can only occur during motor quiescence or the stomach is incapable of contracting during the presence of a tachygastria.

The frequency of the tachygastria (the number of tachygastric ECP's per unit of time) appeared to be rather variable. The highest frequency of the regular tachygastrias observed was 20.6 cpm, the lowest 11.6 cpm. Mostly the frequency was between 13 and 16 cpm, which is about three times the normal gastric frequency.

The frequencies of the much rarer irregular tachygastrias were somewhat lower.

When the frequency of the tachygastria is near the frequency of the duodenal ECA (18 - 20 cpm in the dog), the question arises, of course, whether the tachygastria comes about by retrograde conduction of duodenal ECA into the antrum.

In two dogs tachygastric and duodenal signals could be compared thanks to the presence of a (bipolar) electrode on the proximal duodenum.

Sometimes the frequencies of the signals were very close to one another, but they were never exactly equal. The phase difference between duodenal and antral signal was not constant, not even for short periods.

Mostly the frequency of the tachygastria was lower than that of the duodenal ECA, but sometimes it was slightly higher (Fig.40).

Tachygastrias reaching the pacemaker area were always followed by a compensatory pause of several tens of seconds. This kind of compensatory pause must be of a kind different from the one following single ECP's, since, because of its length, it cannot be understood on the basis of a blockade of conduction.

The duration of the tachygastrias was, by definition, longer than 1 minute. The longest spontaneous tachygastria observed by us had a duration of 59 minutes.

Finally it should be mentioned that in some dogs a psychic influence on the origination of tachygastrias was noticed. Often the tachygastrias occurred at the beginning of the recording sessions, i.e. shortly after handling the animal. In two dogs it was noticed that tachygastrias arose when the animals became frightened during the recording session.

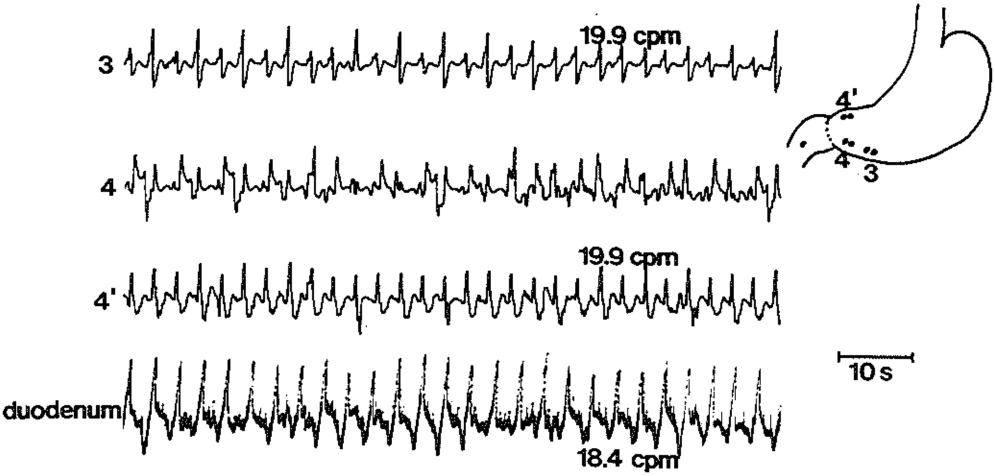

Fig.40 Tachygastria with a frequency higher than the duodenal frequency. There is no constant phase relation between duodenal and antral signals, not even during a short period of time.
Note that the signal from electrode 4 is irregular, whereas the signals from electrodes 3 and 4' are regular. 4' is a bipolar electrode placed at the lesser curvature, opposite electrode 4. The duodenal signal was recorded monopolarly.

4.5.2 Discussion

To our knowledge, the frequent occurrence of ectopic gastric myoelectric activity in the first week after implantation of electrodes was not described previously, although other investigators undoubtedly noticed it. As appears from a personal communication by Sarna, cited by Telander et al. (1978), transient postoperative (and preoperative) gastric arrhythmias also occur in man: 'Sarna has stated that some human gastric arrhythmias recorded during or shortly after operation disappear with recovery'. These findings indicate that arrhythmias found in man during or shortly after an operation are not necessarily related to the disease for which the patient was operated upon.
The mechanisms through which the implantation of electrodes would lead to ectopic impulse formation are yet unclear.

The different configuration of ECP's in monopolar recordings was not described previously either. Some of the illustrations in the publications mentioned in the introduction, however, show ECP's with a similar configuration. For these ectopic depolarizations the cable model seems to be valid to a smaller extent. Possibly, the relative invalidity of this model is connected with a decreased propagation velocity. Sarna and Daniel (1974) reported that premature ECP's (initiated by means of electric stimulation) were propagated more slowly than NECP's. Although this issue was not studied in detail, our recordings seem to confirm this finding (see e.g. Fig.36C).

Code and Marlett (1974) reported that the arrhythmias observed in the stomach of the conscious dog only occurred in phase I of the IMC. We found that ECP's and tachygastrias can also occur during absence of an IMC, and further, that ECP's can also occur during motor activity.

Code and Marlett discerned two types of tachygastria:
- a 'series of coupled beats', in which every NECP was followed by an ECP (frequency therefore about 10 cpm), and
- a (real, regular) tachygastria, with a frequency of about 12 cpm. The highest frequency observed was 12.5 cpm.

In our material series of coupled beats were not observed. The arrhythmia shown in Fig.38 differs from the series of coupled beats described by Code and Marlett by the extremely short interval between the initial potential and the extra potential. In our opinion the arrhythmia of Fig.38 is more likely the extracellular manifestation of the 'secondary spike-like depolarization' described by Daniel (1965) and shown in Fig.11. Apart from its incidence, we are inclined not to use the term tachygastria for the phenomenon of the series of coupled beats.
The frequencies of the tachygastrias in our dogs often were much higher than the highest frequency observed by Code and Marlett (12.5 cpm). The causes of this discrepancy are not clear.
Nevertheless, we agree with Code and Marlett that there are no indications of a possible duodenal origin of tachygastrias. On the contrary, O'Leary and Hennessy (1977) reported that, after resection of an antrum segment in five dogs, 'in two of these animals a duodenal slow wave pattern was recorded 2 cm proximal to the pylorus, indicating retrograde spread into the antral cuff from the proximal duodenum'. When the figure illustrating the phenomenon is analyzed, however, the frequency of the antral electrical activity appears to be 12.2 cpm, whereas the duodenal frequency is 17.4 cpm (both activities are regular). In our opinion the phenomenon observed by O'Leary and Hennessy is not a 'duodenogastria', but a tachygastria.

As mentioned before, Daniel introduced the term *sympathetic dominance pattern* to denote the pattern of gastric myoelectric activity induced with cholinolytic and adrenergic substances, a pattern consisting of absence of second potentials and frequent occurrence of ectopic activity (Daniel 1965, 1966). The effects of adrenergic substances appeared to be mediated by α-receptors.
When it is assumed that in the stomach the effect of α-stimulation comes about through inhibition of acetylcholine release (Daniel, 1966; Daniel and Irwin, 1968; Kosterlitz, 1968), the pattern might also (or better) be called *acetylcholine deficiency pattern.*
Later observations by Sarna and Daniel that corroborate the hypothesis that ectopic impulse formation in the antrum is correlated with low tissue concentrations of acetylcholine are:
- atropine shortens the absolutely refractory period in antral, but not in corporal smooth muscle (Sarna and Daniel, 1974), and
- atropine increases the maximum driven frequency in the antrum (from 7.38 to 9.25 cpm) (Sarna and Daniel, 1973).

Recently an infant with a tachygastria was described in the literature; the child suffered from idiopathic gastric retention (Telander et al., 1978). When tested in vitro, the antral muscle cells of this patient appeared to be far less sensitive to acetylcholine than normal. This observation is in contradiction with the acetylcholine-deficiency-hypothesis. Very recently another possible explanation for human tachygastria was put forward by Sanders et al. (1979). The authors described an adult patient with a tachygastria, whose antral smooth muscle started

to generate normal electrical and mechanical activities in vitro one hour after addition of indomethacin (an inhibitor of prostaglandin synthesis) to the bathing solution. Addition of prostaglandin E_2 to the solution resulted in recurrence of the tachygastria.
The authors concluded that a too high local concentration of endogenous prostaglandin E_2 might be a cause of tachygastria in man.

In the latter two publications mentioned, the intracellular electrical activity of tachygastric smooth muscle was described. This appeared to consist of rapidly recurring depolarizations, absence of plateaus and gradual repolarizations. The repetition frequencies in vitro were 18 to 22 cpm (in the antral tissue of the infant) and 9 to 12 cpm (in the adult).
These observations prove that individual antral smooth muscle cells are capable of generating action potentials at tachygastric frequencies and disprove the (unpublished) hypothesis that alternately firing groups of cells are needed for the generation of a tachygastria.

When a value of 0.6 is taken for the ratio between human and canine ECA frequencies (human stomach 3 cpm, canine stomach 5 cpm; human duodenum 11 cpm, canine duodenum 19 cpm), the in vivo frequency of tachygastria in man should be expected to range from 7 to 12 cpm and to be mostly between 8 and 10 cpm.
The in vivo frequencies of the human tachygastrias reported in the literature were within the expected range, with the exception of the tachygastria in the infant described by Telander et al. (1978), where the in vivo frequency was 5 cpm.

Gastric pacemaker rhythm in conscious dog

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SMOUT, A. J. P. M., E. J. VAN DER SCHEE, AND J. L. GRASHUIS. *Gastric pacemaker rhythm in conscious dog*. Am. J. Physiol. 237(3): E279–E283, 1979 or Am. J. Physiol.: Endocrinol. Metab. Gastrointest. Physiol. 6(3): E279–E283, 1979.—The pacemaker rhythm in the stomach of six healthy conscious dogs was studied by means of the measurement of sequential electrical control activity (ECA) intervals. Only the rhythm originating in the normal pacemaker area was studied. An electrical response activity (ERA) score was used to assess contractile activity. Whereas substantial shortening of nonectopic ECA intervals did not occur, contraction-related interval lengthening was a characteristic phenomenon. The temporal relations between ERA scores and interval durations were found to be dependent on the gastric level at which the signals were derived. The activity front of the interdigestive myoelectric complex (IDMEC) appeared to be correlated with the periodic occurrence of considerably prolonged intervals; this sign could be used for recognition of the IDMEC. The motor quiescence phase of the IDMEC was correlated with small interval-to-interval variation, as was the early postprandial phase.

interdigestive myoelectric complex; electrical control activity; electrical response activity

MANY STUDIES of electrical control activity (ECA) in the canine stomach have been made during the past decennia. Most of these studies paid little regard to the rhythm constituted by the gastric control potentials; in healthy conscious dogs the rhythm is usually described as regular. The widely used parameters "mean" and "standard error of the mean" of the ECA frequency, calculated from the number of control potentials occurring in given periods of time, do not provide much information about ECA rhythm. For a precise description of the rhythm, the laborious measurement of all ECA intervals is a prerequisite.

A prerequisite for any description of gastric ECA is making a choice between the two different views about gastric ECA found in the literature (11, 15). In this study we took the "classical" view that the gastric pacemaker area generates control potentials that are propagated aborally (11). Control potentials originating outside the pacemaker area (ectopic control potentials) were considered phenomena of a different nature and were excluded from the study.

The existence of distinct digestive and interdigestive gastrointestinal motor patterns has been recognized in recent years. Cyclic recurrence of strong contractions in the stomach of the fasted dog has been reported (9); the electrical equivalent of this pattern has been designated the interdigestive myoelectric complex (IDMEC) (5).

The objective of this study is to describe the rhythm of the canine gastric pacemaker and its relation to digestive and interdigestive motor patterns in the conscious dog.

METHODS

Six healthy dogs (Beagles), weighing 8–15 kg, were anesthetized with thiopental sodium (20 mg/kg iv) and maintained at a surgical level of anesthesia with a mixture of oxygen and nitrous oxide (1:2) and enflurane. Four to six bipolar electrodes were sutured to the serosal surface of the stomach using a sterile operating technique. One electrode was additionally placed on the proximal duodenum (4 cm from pylorus) in *dogs 2* and *3*. Each bipolar electrode consisted of two silver/silver-chloride conical tips, 3 mm long, 0.4 mm in diameter, mounted 2 mm apart in a small plate. Four electrode positions along the greater curvature were standard in all six dogs (Fig. 1). Position 1 (12 cm from the pylorus) was chosen because in previous experiments, it appeared to be the most proximal site from which a stable ECA could always be derived.

Electrode signals were transmitted to the recording apparatus by means of either a multipin connector (*dogs 2, 3, 4,* and *5*) or a 6-channel radio transmitter (2) implanted subcutaneously (*dogs 1* and *6*). Bipolar recordings were made on an 8-channel curvilinear chart recorder (Van Gogh EP-8b), using 0.53 and 15 Hz as lower and upper cutoff frequencies. Connections were made so that an upward deflection indicated that the proximal electrode was positive with respect to the distal one. The signals were also recorded on magnetic tape (Racal Store-14), using a tape speed of 15/16 in. per second. Recording sessions began 1 wk after the operation and were continued to up to 6 mo after the operation. No more than two recordings, lasting from 3 to 16 h, were made per week. Signals were derived from all dogs in the fasting state (after a fast of at least 18 h). Recordings were also made with four dogs in the early postprandial phase. When not subjected to fasting, dogs were fed ad libitum (Canex dry food).

The durations of all recorded ECA intervals were measured as follows. The signals were played back from the tape at a speed of 16 times real time, digitized, and fed into a NOVA-2 computer. A program was run that detected ECA peaks and measured the time intervals between them. To reduce the number of detection errors due to artifacts, the detector was made refractory during the first 8 real-time seconds after occurrence of a peak. The interval duration files were checked for errors caused by artifacts and were edited manually. In subsequent

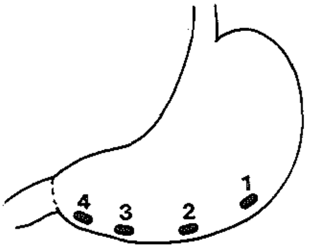

FIG. 1. Positions of electrodes 1–4 at 12, 7, 4, and 2 cm from pylorus, respectively.

data handling, care was taken to exclude ectopic control potentials. Control potentials reaching electrode 1 from above, as indicated by an initial negative deflection in the bipolar registration, were defined as nonectopic. When orally propagated ectopic activity caused a disturbance in the pacemaker rhythm, the first three pacemaker intervals after cessation of the disturbance were also discarded.

In order to investigate the relation between ECA rhythm and motor patterns, an ERA score was used. In this study the term ERA is used to designate both second potentials with spikes and second potentials without spikes. A score of 0 to 3 was assigned to each interval, 0 indicating the absence of ERA (electrical response activity) and 3 indicating intense ERA. The scoring procedure, carried out by visual examination of the chart recordings, is illustrated in Fig. 2. Because of the considerable variability of ERA configuration in the canine stomach, the scoring criteria had to be adapted to each electrode position in each dog. Hence, the method does not permit comparison of scores in different dogs and for different electrode locations.

RESULTS

All animals remained healthy throughout the study. Especially in the first weeks after operation, tachygastrias (tachyantrias) were encountered in *dogs 1, 3,* and *5*. Single ectopic control potentials occurred in all dogs but *dog 2*. Almost continuous ectopic activity was present in the antrum of fasted *dog 3*. Interdigestive myoelectric complexes were observed in the stomachs of only three of our fasted dogs (*dogs 4, 5,* and *6*). In these dogs the activity fronts of gastric IDMEC were never characterized by the presence of maximum ERA with each control potential; the succession of ECA intervals with maximum ERA was periodically interrupted by intervals with low or absent ERA. Caudad migration of interdigestive complexes was not observed in the stomach. In *dogs 1, 2,* and *3* no substantial periods of motor quiescence occurred in the fasted state; instead irregular ERA was continuously present. However, myoelectric signals simultaneously derived from the small intestine of *dogs 2* and *3* clearly showed IDMEC.

When gastric interdigestive complexes occurred, their presence could be recognized from plots of interval durations versus time (interval functions). As illustrated in Fig. 3, the activity fronts were correlated with groups of sharp peaks in the interval function, whereas the interval-to-interval variation during the quiescent phase was relatively small. Dips in the interval functions were rare and only occurred immediately before a large peak.

As mentioned before, *dogs 1, 2,* and *3* showed no gastric IDMEC. The interval functions of *dogs 1* and *3* showed occasional peaks in the fasted state that were contraction-related as described above.

The peaks in the interval function covered 3–7 intervals (40–85 s). Peak amplitudes of up to 30 s were observed. Two extreme peak onset configurations are depicted in Fig. 4. In Figure 4*A* the largest interval is preceded by a prolonged interval, whereas in Fig. 4*B* the largest interval is preceded by a short interval. As illustrated in Fig. 5, the amplitudes of peaks decreased from body to antrum by a small percentage; in other words, control potentials occurring after a prolonged interval were propagated faster. This phenomenon also manifested itself in the difference between the standard deviations of interval durations obtained from antrum and body (Fig. 6). When no peaks were present, the standard deviations in antrum and body were equal.

More detailed studies of the relation between interval durations and ERA scores revealed that, at the level of electrode 1, peaks in the interval function coincided with high ERA scores. At the level of electrode 4, the peak interval was without ERA in about 50% of the cases, whereas the interval just before it showed high ERA (Fig. 7). When the dogs were fed after a period of fasting and the digestive state set in, interval durations lengthened and the interval-to-interval variation decreased (Fig. 8). Peaks were not observed in this state.

DISCUSSION

Interval analysis of gastric control potentials and contractions has been advocated since 1965 by Nelsen and his co-workers (13, 14) and recently by Hiesinger et al. (8). Our study differs from the above-mentioned studies in excluding ectopic activity, in considering the differences caused by recording from different gastric levels

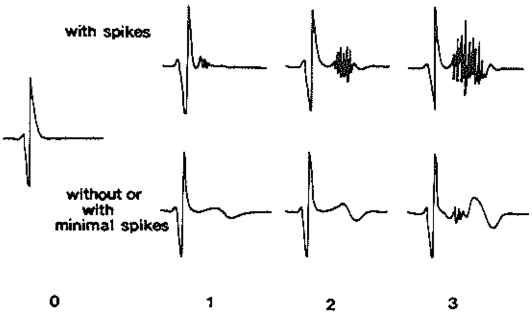

FIG. 2. ERA scores (examples). In tracings with spikes (upper set of examples) ERA was scored higher as duration and amplitude of spike train increased. In tracings without spike activity or with minimal spike activity (bottom set) ERA was scored higher as duration of interval between initial and second potential and second potential amplitude increased.

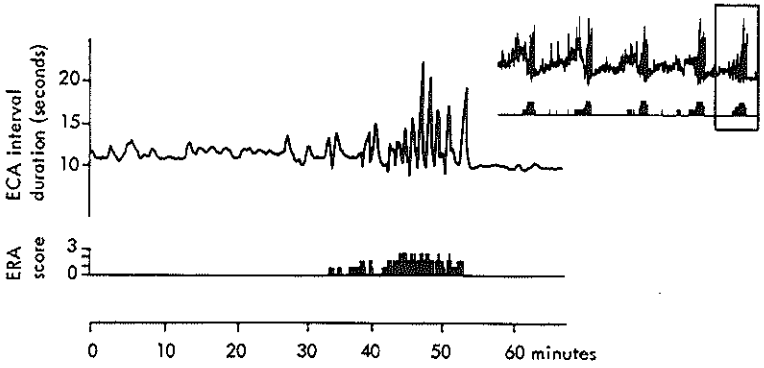

FIG. 3. Interval function (electrode 1) and plot of ERA scores showing an IDMEC cycle that is last of 5 cycles shown in inset (*dog 6*).

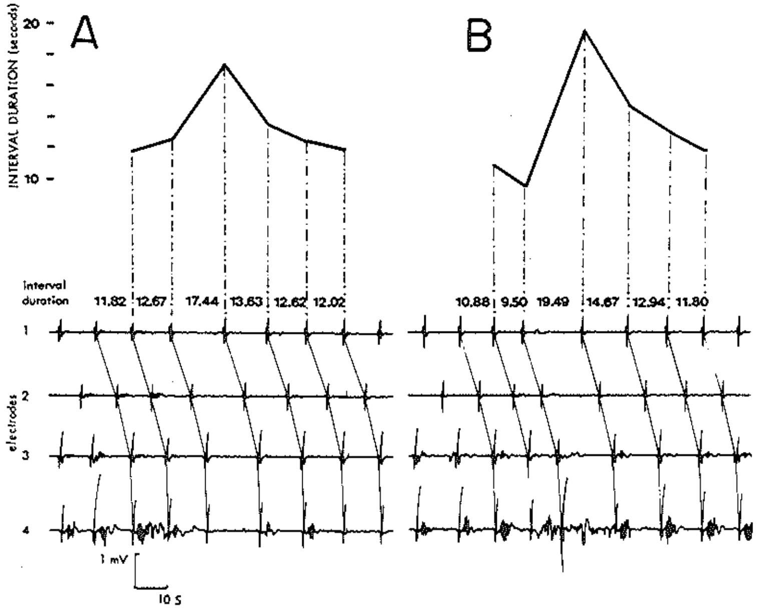

FIG. 4. Two extreme peak onset configurations (*A* and *B*) observed in interval functions (upper part) and corresponding myoelectrical signals (lower part).

and in discussing the relation between ECA rhythm and IDMEC.

Hiesinger et al. (8) stated that the (antral) ECA intervals following isolated contractions were lengthened. Our results, however, show that the relation between ERA score and duration of the corresponding ECA interval depends on the gastric level at which the signals are derived. As a rule, at the corporal level the intervals with high ERA scores were prolonged, whereas at the antral level the intervals following high ERA were lengthened. This difference can be understood by realizing that control potentials are propagated, whereas ERA is not (6).

Gastric IDMEC, when present, could be recognized from the interval function by the considerably prolonged intervals that coincide with the strong contractions of the activity front. Recently activity front-related interval prolongation was also noticed by Mroz and Kelly (12).

Another characteristic of gastric IDMEC encountered in this study is the periodic occurrence of ECA intervals with low to absent ERA during the activity front. In contrast, Code and Marlett (5) described the activity front as characterized by the presence of maximum ERA with each control potential. Our observations, however, are in accordance with the description of the motor correlate of the activity front in the canine stomach, given by Itoh et al. (9).

In half our dogs gastric IDMEC was absent. Theoretically this absence could be ascribed to many different causes. Absence of intestinal IDMEC has been observed in relation with partial bowel obstruction and distemper (3), inadequate fasting periods (16), delayed gastric emptying after truncal vagotomy (1), and bacterial overgrowth of the small intestine (17). However, because of the presence of intestinal interdigestive complexes during

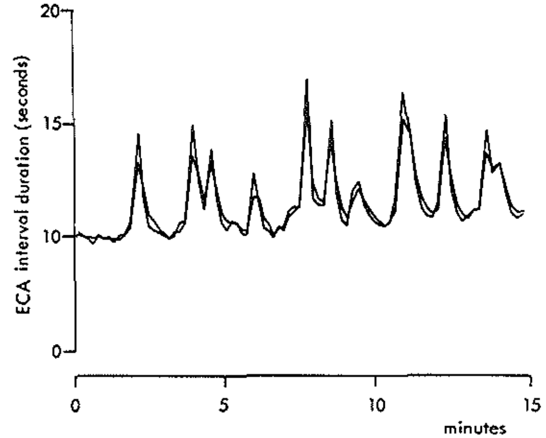

FIG. 5. Corresponding interval functions obtained from electrodes 1 and 4 projected in 1 figure. Interval function with highest peaks was derived from electrode 1 (*dog 4*, fasted, no IDMEC present).

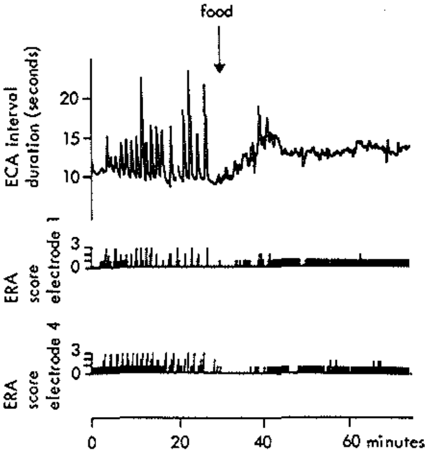

FIG. 8. Interval function and plot of ERA scores (electrodes 1 and 4) illustrating effect of feeding (arrow) (*dog 4*).

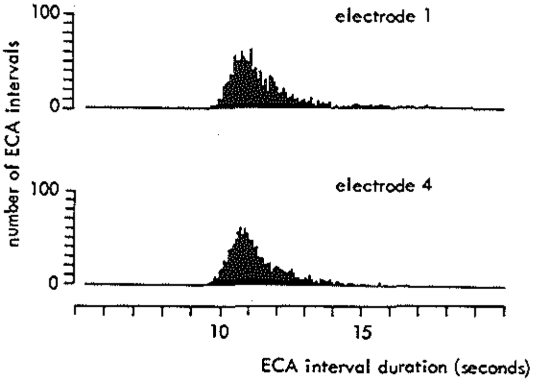

FIG. 6. Distributions of 1,232 corresponding intervals derived from electrodes 1 and 4 in fasted *dog 4* during absence of IDMEC. Electrode 1: mean 11.35 s, SE 1.36 s (n = 1,232). Electrode 4: mean 11.35 s, SE 1.09 s (n = 1,232).

absence of gastric IDMEC, in *dogs 2* and *3*, we would like to suggest that gastric IDMEC in general is not as stable as its intestinal counterpart. Observations in man corroborating this suggestion were made by Catchpole and Duthie (4) and by Vantrappen et al. (17). Itoh et al. (10) reported that in their dogs not all interdigestive complexes started in the stomach.

The observed ERA-related variations of gastric ECA rhythm indicate that gastric ECA is not only an autonomous, omnipresent oscillatory process that controls phasic activity, but that it is also controlled itself. If we consider the gastric pacemaker area as a pulse generator, as we did in this study, pulse-frequency modulation obviously occurs. It must be noted that this frequency modulation is only in one direction; substantial shortening of intervals does not occur. In our opinion this latter finding indicates that the pacemaker area usually oscillates at or near its maximum frequency.

A last conclusion to be drawn from our material is the relative unsuitability of parameters like the mean and

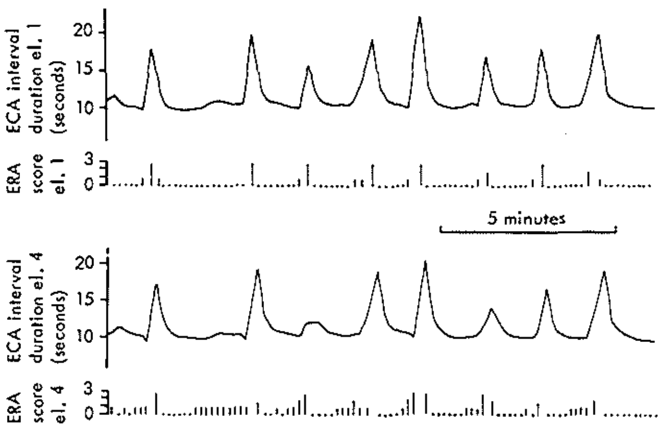

FIG. 7. Interval functions and plots of ERA scores obtained from electrode 1 and 4 showing coincidence of peaks with high ERA scores at level of electrode 1. Corresponding intervals are plotted in line (*dog 4*, fasted, activity front).

standard deviation of ECA interval duration. Especially in the fasted state, in which a variable number of prolonged intervals gives rise to a variable skewing of the interval distributions, means and standard deviations are of very limited significance. These parameters were therefore not routinely included in this paper.

The animal experiments were carried out at the Erasmus University Laboratory for Experimental Surgery, which is under the direction of Dr. D. L. Westbroek.

Received 28 August 1978; accepted in final form 17 April 1979.

REFERENCES

1. AEBERHARD, P., AND B. S. BEDI. Effects of proximal gastric vagotomy (PGV) followed by total vagotomy (TV) on postprandial and fasting myoelectrical activity of the canine stomach and duodenum. *Gut* 18: 515–523, 1977.
2. BESSELING, N. C., D. CH. VAN MAAREN, AND Y. J. KINGMA. An implantable biotelemetry transmitter for six differential signals. *Med. Biol. Eng.* 14: 660–664, 1976.
3. CARLSON, G. M., B. S. BEDI, AND C. F. CODE. Mechanism of propagation of intestinal interdigestive myoelectric complex. *Am. J. Physiol.* 222: 1027–1030, 1972.
4. CATCHPOLE, B. N., AND H. L. DUTHIE. Postoperative gastrointestinal complexes. In: *Gastrointestinal Motility in Health and Disease*, edited by H. L. Duthie. Lancaster, England: MTP Press, 1977, p. 33–41.
5. CODE, C. F., AND J. A. MARLETT. The interdigestive myoelectric complex of the stomach and small bowel of dogs. *J. Physiol. London* 246: 289–309, 1975.
6. DANIEL, E. E. The electrical and contractile activity of the pyloric region in dogs and the effect of drugs. *Gastroenterology* 49: 403–418, 1965.
7. DANIEL, E. E., AND S. K. SARNA. Distribution of excitatory vagal fibers in canine gastric wall to control motility. *Gastroenterology* 71: 608–613, 1976.
8. HIESINGER, E., H. HOERNICKE, AND H. J. EHRLEIN. Computer analysis of electrical and mechanical activity of stomach, duodenum and cecum over long periods. In: *Gastrointestinal Motility in Health and Disease*, edited by H. L. Duthie. Lancaster, England: MTP Press, 1977, p. 275–284.
9. ITOH, Z., I. AIZAWA, S. TAKEUCHI, AND R. TAKAYANAGI. Diurnal changes in gastric motor activity in conscious dogs. *Am. J. Dig. Dis.* 22: 117–124, 1977.
10. ITOH, Z., S. TAKEUCHI, I. AIZAWA, AND R. TAKAYANAGI. Characteristic motor activity of the gastrointestinal tract in fasted conscious dogs measured by implanted force transducers. *Am. J. Dig. Dis.* 23: 229–238, 1978.
11. KELLY, K. A., AND C. F. CODE. Canine gastric pacemaker. *Am. J. Physiol.* 220: 112–118, 1971.
12. MROZ, C. T., AND K. A. KELLY. The role of extrinsic antral nerves in the regulation of gastric emptying. *Surg. Gynecol. Obstet.* 145: 369–377, 1977.
13. NELSEN, T. S., E. H. EIGENBRODT, AND L. A. KEOSHIAN. Motor responses of the canine stomach to insulin and feeding. *Arch. Surg.* 92: 379–385, 1966.
14. NELSEN, T. S., AND J. M. WALLACE. An instrumentation system for on-line processing and statistical analysis of electroenterographic and electrogastrographic data. *Proc. Conf. Med. Electron. Biol. Eng., 6th, Tokyo*, 1965.
15. SARNA, S. K., E. E. DANIEL, AND Y. J. KINGMA. Simulation of the electric control activity of the stomach by an array of relaxation oscillators. *Am. J. Dig. Dis.* 17: 299–310, 1972.
16. TAKEUCHI, S., AND Z. ITOH. A problem concerning intragastric pressure measurement in conscious dogs. *Gastroenterology* 72: 1367, 1977.
17. VANTRAPPEN, G., J. JANSSENS, J. HELLEMANS, AND Y. GHOOS. The interdigestive motor complex of normal subjects and patients with bacterial overgrowth of the small intestine. *J. Clin. Invest.* 59: 1158–1166, 1977.

4.7 *Conclusions*

- The monopolar serosal signal consists of a cyclically recurring, positive-negative 'inital potential', which may be followed by a contraction-related negative-positive 'second potential'. The segment between the two potentials, the 'interpotential segment' is negative and may exhibit rapid oscillations, called spikes.
- The configuration of the monopolar signal can be understood by assuming that it consists of two components: a component resembling the second time derivative of the intracellular signal, and a component resembling the inverted intracellular signal. In the antrum the former component predominates, in the corpus the latter is predominant.
- With increasing amplitude of the second potential and with increasing duration of the interpotential segment, the amplitude of the phasic contraction increases. Absence of the second potential indicates motor quiescence. These findings are in accordance with results of intracellular studies.
- Recording from freely moving animals is much easier with bipolar than with monopolar techniques.
- The bipolar signal can best be regarded as the difference between two monopolar signals.

- Ectopic Control Potentials (ECP's), arising from a focus outside the normal pacemaker area, are either signle or repetitive.
  Single ECP's are either interpolated or are followed by a compensatory pause.
- The inclination towards the generation of ECP's increases towards the pylorus.
- Tachygastrias are not due to retrograde spread of duodenal activity into the stomach.
- The repetition frequency of tachygastric potentials varies from 12 to 20 cpm, but usually is between 13 and 16 cpm, which is about three times the normal gastric frequency.
- Tachygastrias can be induced by psychic stimuli.
- The activity front of the interdigestive myoelectric complex (IDMEC) is correlated with the occurrence of considerably prolonged ECA intervals.
- The motor quiescence phase of the IDMEC and the early postprandial phase are correlated with small interval-to-interval variation.
- The temporal relations between contractions (ERA scores) and ECA interval duration depend on the gastric level at which the signals are derived.
- Substantial shortening of nonectopic ECA intervals does not occur.
- The activity front of gastric IDMEC is not characterized by the presence of maximum ERA with each control potential; the succession of ECA intervals with maximum ERA is periodically interrupted by intervals with low or absent ERA.
- Gastric IDMEC is not as stable as its intestinal counterpart.

5. ELECTROGASTROGRAPHY

5.1 *Introduction*

Many internal organs are known to bring about potential variations at the surface of the body.

The method of recording from the skin the potential variations generated by the heart (electrocardiography, ECG or EKG) has become a very important aid in the diagnosis of cardiac disorders.

Other 'EXG'-methods also proved to be of clinical importance.

In the chapters 3 and 4 we saw that the stomach, an organ that contains a considerable mass of smooth muscle, generates electrical signals. As will appear from this part of the thesis, information about the electrical behaviour of the stomach can also be obtained by means of recording skin potential variations. The method of recording skin potential variations generated by the stomach can be designated *electrogastrography* (EGG).

5.2 *Chronological literature survey*

This survey will be restricted to publications in which signals recorded from the skin are discussed. Publications in which the term 'electrogastrography' is used, but deal with intraluminally or serosally recorded signals, will not be discussed.

On October 14, 1921 Walter Alvarez recorded the first electrogastrogram in a thin, elderly woman with a large cicatricial hernia.

Fig. 41 shows the positions of the electrodes and the signal obtained.

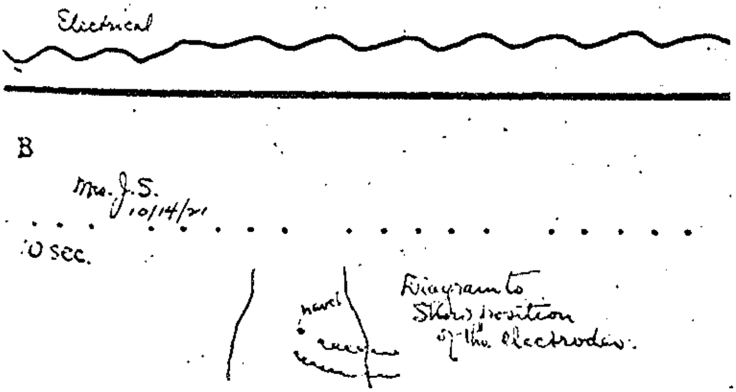

*Fig.41 The first electrogastrogram, recorded by Alvarez.
The intervals between the dots represent 10 seconds.*

The recorded signal resembled a sine wave ('sinusoidal' configuration), its frequency was 3 cpm. The peristaltic contractions of the stomach, which could be seen through the skin, corresponded with the recorded potential variations, so that the gastric origin of the electrogastrographic signal could be established without doubt (Alvarez, 1922, 1968).
Alvarez reported however, that he never succeeded in recording electrogastrograms from other persons.

In 1953 Ingram and Richards published results of measurements of the secretion-related potential differences (PD) between gastric lumen and forearm in man. The authors also measured potential differences between electrodes placed on the skin. Unfortunately, results of these latter measurements were not provided.

In 1957 Davis et al. reported on their 'Exploration of Abdominal Potentials' in man. Potential differences between two electrodes placed on the abdominal skin, as well as between one electrode on the abdomen and one at a 'neutral point' were explored.
The authors recorded sinusoidal signals with a frequency of about 3 cpm. Various artifacts were excluded as possible sources of these signals. Gastric movements were recorded simultaneously with the help of a swallowed piece of steel and a mine detector mounted under the couch. The authors concluded that the 3 cpm component of the cutaneous signal is an electrical correlate of the phasic contractions of the stomach.

In 1959 Tiemann and Reichertz published on the 'Electrointestinogram' (Tiemann and Rechertz, 1959a, 1959b). In these publications also some results of electrogastrographic explorations (in man) are reported. The authors used a technique with one electrode on the abdomen and one on the right leg. In normal subjects waves with a frequency of 3 cpm were recorded. It was stated that affections of the gastrointestinal canal were often accompanied with changes in the signals recorded from the skin, but clear descriptions of these changes were not given.

In 1962 Sobakin et al. reported on their experiences with the electrogastrograph in healthy volunteers and in patients with various gastric disorders. The authors used a technique with one electrode in the epigastric region and one on the right leg. All recordings were made in the digestive state after consumption of a test meal.
In the healthy subjects a frequency of 3 ± 0.3 cpm was found. The amplitude of the gastric wave usually reached 250 µV. In fat subjects electrogastrography appeared to be possible as well.
In patients with pyloric stenosis the amplitude of the gastric waves was increased. In patients with gastric carcinoma (presumably in an advanced stage) waves with a highly varying rhythm ('poikiloperistalsis') were seen.

The studies on the gastric signals recorded from the skin of the goat published by Itabisashi and Matsumoto (Itabisashi, 1964a, 1964b, 1965; Itabisashi and Matsumoto 1964, 1966) do not show any correspondence to the rest of the electrogastrographic literature.

In 1967 Russell and Stern contributed to 'A manual of Psychophysiological Methods' with a chapter on electrogastrography. Most of the data presented in that chapter are the same as in the above-mentioned publication by Davis et al., (1957).
An experiment in the dog is described, in which intraluminal, serosal and cutaneous electrical signals of the stomach were recorded simultaneously. The authors stated that 'a significant positive correlation was obtained

between the gastric activity of the three sites', but a figure showing the three signals completely fails to corroborate this statement.

In 1967 Nelsen described the use of phase-lock techniques for the filtering of (human) electrogastrographic signals. Nelsen was of opinion that these techniques made it possible to obtain gastric signals from a majority of patients without resorting to invasive techniques.
In 1968 Nelsen and Kohatsu described their experiences with gastroelectromyography and electrogastrography in man. The authors briefly returned to the use of phase-lock systems, but did not present new information. The publication contains a figure however, that graphically shows the effect of feeding on gastric frequency in dog and man. The interesting facet of that figure is that the human frequencies were determined from cutaneous signals (be it in one subject).

Since 1967 numerous publications by Martin, Thillier, Martin and co-workers (Tours, France) saw the light. Most of these publications dealt with studies in man and contained about the same information.
The French group of investigators is not only engaged in electrogastrography, but claims to record small intestinal and colonic activity from the skin as well. The group uses the term 'electrosplanchnography' for recording from electrodes on the abdomen, and the term 'electrogastroenterography' for recording from electrodes on the limbs, and alleges that the latter method has several advantages: greater reliability of amplitude criteria, smaller dependency on the positions of the internal organs, smaller dependency on the thickness of the abdominal fat layer and less time-consuming attaching of the electrodes (Martin and Thillier, 1971a).
The time constant of the high-pass filter used is 3 or 6 seconds. The cut-off-frequency of the low-pass filter is not reported in any publication by the French group, but it is probably higher than 10 Hz, since the signals shown contain large QRS complexes.
Depending on the positions of the electrodes, the direction of the axis connecting the electrodes and the time of the day, the French group observes:
- gastric activity; frequency about 3 cpm,
- small intestinal activity; frequency 7 to 12 cpm, and
- colonic activity, which is aperiodic and is characterized by large, biphasic or triphasic potential variations, occurring one time per minute or less (Martin et al., 1967).

Radiocinematographically an excellent correlation between the motor activities of the alimentary canal and the recorded electrical signals is alleged to be found, but relevant investigations were never published.
The authors regard the signals recorded from the skin as a reliable measure of the contractile activities of the gastrointestinal canal and take the view that absence of (visually recognizable) waves implies absence of contractile activity.
Until recently, experimental confirmation of these assumptions was not pursued. Recently, an investigation into the relations between electrogastrographical and gastroelectromyographical signals and intragastric pressure in the guinea-pig was performed (Drieux et al., 1978). The investigators concluded that 'the origin of EGEG (electrogastroenterogram) is essentially the movements of the stomach', but were unable to elucidate the mechanism by which the relation between gastric movements and surface potential variations comes about.
In analogy with vectorcardiography, Martin and Thillier attempted to introduce vectorgastrography and even vectorjejuno-, ileo- and colography, using limb electrodes (Martin and Thillier, 1971b; Martin and Thillier, 1972). Instead of the triangle of Einthoven, a trapezium is used, the angular points of which represent the junctures of the extremities to the trunk.

Apart from the question whether the construction of a vectorgastrogram is theoretically permissible, the authors' conclusions regarding the vectorgastrographic determination of the positions of the anatomical axes of corpus and antrum must be considered premature at the least.
The French group claims that the methods of electrosplanchnography and electrogastroenterography are ofgreat diagnostic importance. In 1971, for example, Martin et al. described the electrogastrographical detection of an infiltrating carcinoma of the terminal antrum that had been missed at radiological examination. The electrogastrographic abnormalities consisted of an hyperactivity in the epigastric region (amplitude 300 µV, frequency 3 cpm) and a total absence of activity in the right hypochondriac region, which, according to the authors, oughts to reflect the activity of the pylorus. The following electrogastrographic diagnosis was issued: 'lésion anatomique de la région antro-pylorique dont l'activité électrique ne se manifeste plus (infiltration, fibrose ou paralyse par phénomènes hémorrhagiques)' [⊠].
Other diagnostic successes were claimed to be reached in psychosomatic disorders of the alimentary canal (Martin et al., 1970), in post-vagotomy states (Martin et al., 1972) and in diarrhoea, pyloric stenosis, constipation and psychogenic vomiting in infants (Combe et al., 1972). According to the latter authors, for that matter, the frequency of the infantile stomach is the same as in the adult stomach.
More recent studies, particularly those which were made in collaboration with Tonkovic (Yugoslavia), and in which the method of spectral analysis was used, make a more realistic impression (Thouvenot et al., 1973; Tonkovic et al., 1975; Tonkovic et al., 1976). In healthy, fasting volunteers a gastric frequency of 2.7 to 3.6 cpm was found. The peak-to-peak amplitude of the gastric waves was 180 to 450 µV. The signals alleged to come from the duodenum had a frequency of 11.2 to 13.0 cpm and an amplitude of 45 to 106 µV.

In 1973 Nechiporuk et al. reported (in Russian) that in 47 patients with acute pancreatitis and in 20 patients with acute 'cholecystopancreatitis' a significant suppression of the electrogastrographic activity was observed. The authors recommended electrogastrography as 'an additional, objective diagnostic and prognostic test' in pancreatitis.

In the same year Schulz et al. (1973) published some results obtained with the techniques of the French group. Both extremity and abdominal leads were used. The authors established that the signals recorded from the extremities were less conclusive. Intravenous administration of metoclopramide resulted in an increase of amplitude and frequency of the gastric waves.

In 1976, Schulz et al. described the effects of some drugs on gastric motility, studied with electrogastrography. Metoclopramide increased, atropine decreased the frequency of the gastric waves (from 3.36 ± 0.2 to 5.45 ± 0.3 and from 3.51 ± 0.2 to 2.93 ± 0.2 cpm, respectively). The authors considered it to be conceivable that electrogastrography as 'pharmacological function test' yields valuable diagnostic information.

In 1974 Stevens and Worrall reported on their electrogastrographic studies in the cat. The signals obtained from the skin (with one electrode on the abdomen and one on the left hind leg) were compared with those obtained

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[⊠] 'anatomic lesion of the antropyloric region, the electrical activity of which is not present any more (infiltration, fibrosis or paralysis by hemorrhagic phenomena)'.

from an extraluminal force transducer attached to the stomach. In the analysis of the signals, hand methods as well as auto- and cross-correlation techniques and Fourier transforms were used. With these techniques, a periodical component with a frequency of 3.76 to 4.54 cpm was found (in the cat the gastric frequency is about 4 cpm). Furthermore, significant correlations between the cutaneous signal and the contraction signal were found (correlation coefficients above 0.80).
The authors stated, however, that the correlation was not perfect, and that 'one can find segments of record where slow wave electrical activity appears to occur in the presence of a quiet mechanical record'.

In 1975 Brown et al. (Sheffield, England) published the results of a study in sixteen healthy volunteers. The investigators used a bipolar abdominal recording technique.
Fourier Analysis, auto- and cross-correlations were applied for analysis. In a few cases mucosal gastroelectromyographic signals were recorded simultaneously and intragastric pressure was measured.
In 88% of the signal fragments analyzed a significant component with a frequency of around 3 cpm (3.02 ± 0.21 cpm) was found.
The following possible sources for this component were mentioned by the authors:

1. electrode artifacts,
2. an unknown intra-abdominal 3 cpm oscillator,
3. mechanically artifacts caused by the contractions of the stomach, and
4. the electrical control activity of the stomach, called 'BER' by the authors.

On the basis of several arguments, Brown and colleagues (1975) concluded that possibility 4 is the (only) correct one. Possibility 3 (mechanical artifacts) was excluded on the basis of:

- the consistency of the gastric waves in the cutaneous signals (contractions do not occur continuously, the electrogastrographic signal does) and
- the presence of a 3 cpm component in the cutaneous signal during absence of mechanical activity.

In 9 out of 32 recordings (especially in the fasted state) a periodic component of a higher frequency (10 to 12 cpm) was found. This component was considered to arise from the small intestine.
After consumption of a meal the amplitude of the gastric component increased with about 150%. This increase was assumed to be due to a decreased distance of the electrodes to the distended stomach.

The Sheffield group further published results of several studies into the methods of analysis of electrogastrographic signals (Smallwood et al., 1975; Smallwood, 1976, 1978a, 1978b; Linkens, 1977). To these methods belong Fast Fourier Transform, Fast Walsh Transform, autoregressive modelling, phase-lock techniques, autocorrelations and crosscorrelations.
The thesis of Smallwood (1976) contains, besides some of the above-mentioned matters, results of measurements on patients before and after truncal vagotomy plus pyloroplasty. Some significant differences between mean gastric frequencies in the different groups were found, but the overlaps were such that the results loose much of their importance.
Highly interesting however, are the postprandial frequency changes observed in the control groups of healthy volunteers. Immediately after a meal the frequency decreased significantly, to be followed by an increase in frequency to above the fasting value. Similar postprandial frequency drops followed by a rise had been observed earlier by Nelsen and Kohatsu (1968) (with the help of electrogastrography) and by Duthie et al. (1971) (with the help of serosal electrodes).

In 1976 Sobakin and Privalov described their 'multichannel' EGG-technique, in which a great number of electrodes is placed on the abdomen and one neutral electrode on the right leg. Auto-correlation functions of all signals thus obtained were calculated.
The mean gastric frequency of healthy volunteers after a test meal was 3.0 ± 0.1 cpm. The signals recorded from the various electrodes were closely correlated.
During the first 15 minutes after the meal the amplitudes of the signals from electrodes above cardia, fundus and corpus were higher than those from electrodes above the distal stomach (the positions of the electrodes were verified fluoroscopically). Later after the meal the ratio of the amplitudes inverted.
Sobakin and Privalov interpreted these results as follows: shortly after a meal the peristaltic waves become weaker towards the pylorus, whereas later after a meal the peristaltic contractions of the distal stomach are stronger than those of the proximal stomach. Evidence supporting this interpretation was not provided.

The publications by Walker and Sandman (1977) and Walker et al. (1978), dealing with psychogenic effects on abdominal skin potentials (recordings of which are called electrogastrograms by the authors), completely ignore the relation of these potentials with gastric function.

In 1978 Colombo et al. reported (in Italian) their experiences with cutaneous recordings in patients with obstructions in the gastro intestinal canal. The exploring electrodes were placed at different locations on the abdominal skin, the indifferent electrode was composed of electrodes placed on both arms and on the left leg. The recording sessions lasted only 10 minutes.
In patients with pyloric stenosis, waves with a frequency of 3 cpm were seen in the cutaneous signals, especially in those recorded from the epigastric region. The amplitude of these waves was 0.2 to 0.7 mV. In patients with an obstruction of the small intestine, the dominant frequency was 7 to 12 cpm (amplitude 0.2 to 0.5 mV), and in patients with an obstruction of the colon the polyphasic complexes described by the French group were observed.
In patients with paralytic ileus, the cutaneous recordings were flat.

Finally it should be mentioned that Taylor et al. (1975) reported that the (human) colon generates two types of periodical electrical activity, one with a frequency of about 3 cpm, the other with a frequency of 6 to 11 cpm. Both types were recorded from the mucosa, from the serosa and from the skin. Since all signals were recorded with monopolar techniques, since the two types of activities had similar incidences in the signals recorded from all three sites, and since the amplitudes of the signals from all three sites were approximately equal, the colonic origin of these signals might be doubted.

The literature on electrogastrography can be summarized as follows:

Since 1921 a limited number of attempts has been made to record electrogastrographic signals. In most of these attempts only external electrodes were used and no reference signals from the stomach itself were obtained. Nevertheless, it has become clear that the sinusoidal 3 cpm signal that can be recorded best from the epigastric region, is of gastric origin.
Most authors dealing with electrogastrographic signals assumed that these signals reflect the motor activity of the (distal) stomach; during absence of peristaltic activity the cutaneous signal was considered not to contain a 3 cpm component. In contrast, Brown et al. (1975) concluded that in electrogastrography the electrical control activity of the stomach is

measured, implying that a 3 cpm component is present during motor quiescence as well.
The mechanism through which the electrogastrographic signal comes about is still completely unclear.
On the basis of the literature presently available, the possible clinical relevancy of electrogastrography can hardly be estimated. Unfortunately, all publications in which diagnostic applicability of the method was claimed are little convincing.

5.3 Pilot experiments regarding the technique of electrogastrography

5.3.1 Introduction

In principle, the technique of electrogastrography is simple. The potential difference between electrodes attached to the skin is amplified, filtered and recorded (on paper, magnetic tape or both).

Since the fundamental gastric frequency of the electrogastrographic signal is very low (0.05 Hz in man and 0.08 Hz in the dog), and since the *electrode impedance* and the *electrode noise* increase with decreasing frequency (Geddes and Baker, 1968; Geddes, 1972), it was considered necessary to investigate which kind of electrode would be most suitable for electrogastrographic purposes.

As in electrocardiography, five main types of *leads* can be used in electrogastrography (Fig.42).

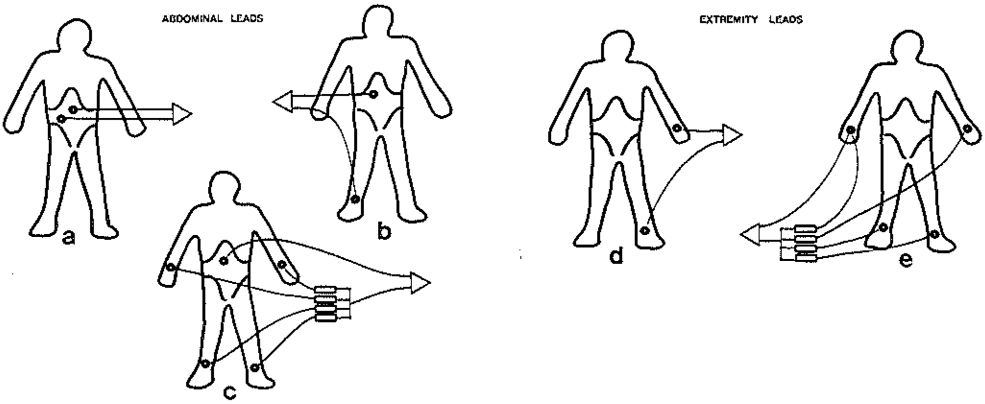

Fig.42 The five electrogastrography leads:

abdominal leads:
- *bipolar (a)*
- *unipolar with respect to an extremity (b)*
- *unipolar with respect to 'central terminal' (c)*

extremity leads:
- *bipolar (d)*
- *unipolar with respect to 'central terminal' (e)*

A choice between these types of leads had to be made.

Finally, the bandwidth of the amplifiers had to be chosen.

5.3.2 Methods and results

The noise produced by several types of commercially available electrodes (for the greater part electrocardiography electrodes) was studied. The potential difference between pairs of identical electrodes with interposed electrolyte-containing gel (Redux Paste, Hewlett Packard) was amplified and recorded on paper.
It was concluded that some of the disposable, pregelled Ag/AgCl ECG electrodes were sufficiently 'quiet' to serve as electrogastrographic electrode. These electrodes, e.g. Hewlett Packard 14245A, Harco type 155, 3M type Red Dot, all are 'recessed', i.e. the metal of the electrode proper is built in a small basin filled with a gel-containing sponge.
The impedance of pairs of Hewlett Packard 14245A electrodes, which were used in our studies, was measured. Only total impedance, consisting of a capacitive and a resistive component, was measured (Fig.43).

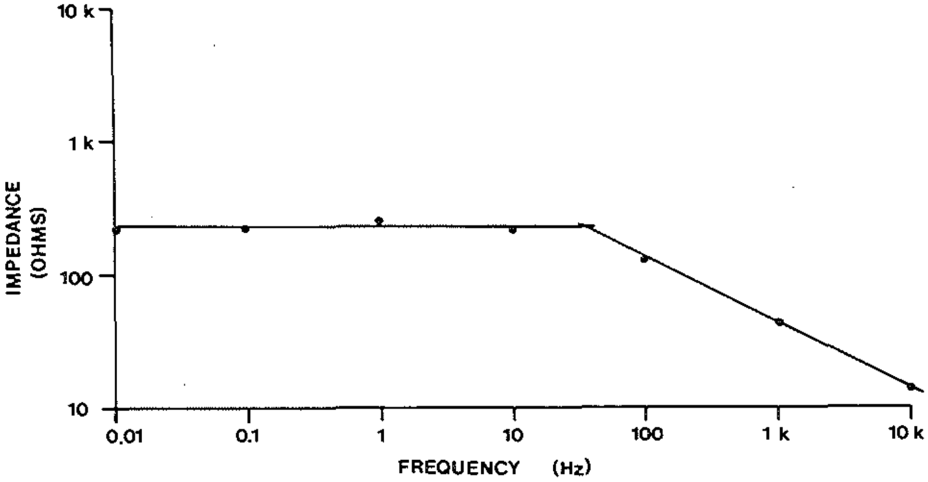

Fig.43 Total impedance (in ohms) versus frequency (in Hz) of a pair of Hewlett Packard 14245A electrodes with interposed electrolyte gel. Surface of the electrodes 52 mm^2. Impedances measured with a current of 10 μA.

At frequencies below 10 Hz the electrode impedance appeared to be frequency-independent. At these frequencies the impedance of one electrode-electrolyte interface appeared to be approximately 100 Ω. Subsequently, the impedances between electrodes placed on the human and canine skin were measured. Typical plots are shown in Fig.44.
By thorough abrasion, the impedance of the electrode-electrolyte-skin-body-skin-electrolyte-electrode system could be reduced to less than 10 kΩ.

Both in man and in the dog, the bipolar abdominal leads appeared to yield the signals with the highest signal-to-noise ratio. As illustrated in Fig.45, most of the artifacts present in unipolarly recorded signals were absent in the bipolar abdominal leads.

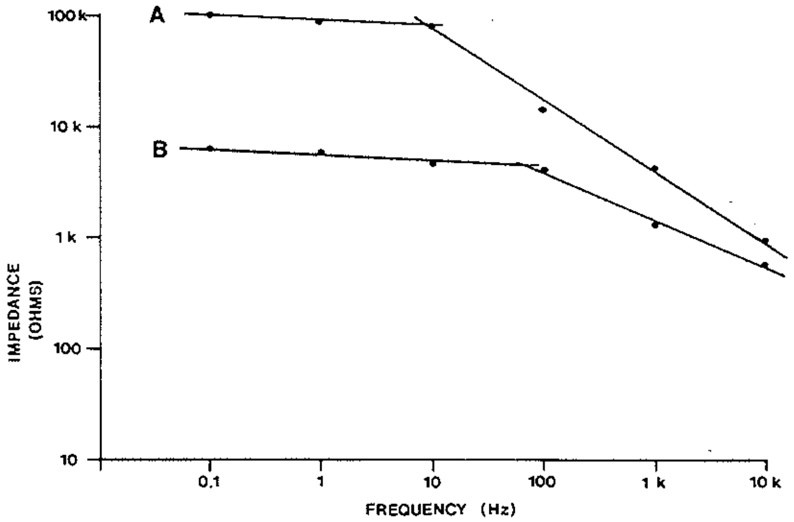

Fig.44 Total impedance of a pair of Hewlett Packard 14245A electrodes on the human leg versus frequency.

A: electrodes placed on unabraded skin,
B: electrodes placed on skin abraded with Redux Paste (Hewlett Packard).

In the dog similar values were found.

The use of low-pass filters with a cutoff-frequency of about 0.5 Hz was found to be practical, since with these filters most of the electrocardiogram was eliminated. An additional advantage of the use of such a low cutoff-frequency appeared to be that it made the recording method very insensitive to 50 (or 60) Hz interference.
Because of the presence of DC electrode potentials and electrode drift, high-pass filtering appeared to be necessary. A cutoff-frequency of about 0.015 Hz appeared to be the lowest cutoff-frequency practical.

5.3.3 Discussion

In the case of an abraded skin, the impedance of the electrode-electrolyte-skin-body-electrolyte-electrode system at very low frequencies was found to be about 10 kΩ.
The major part of this impedance is due to the impedance of the skin, since the two electrode impedances are approximately 200Ω and the impedances of all other tissues are relatively low (Geddes and Baker, 1967). From the comparison of the figures 43 and 44 it can be concluded that the impedance of the skin, like the electrode impedance, is frequency-dependent. Fig.44 shows that the effect of abrasion on skin impedance is greatest at frequencies below 10 Hz. These findings are in accordance with those made by Swanson and Webster (1974).
The impedance values found at lower frequencies (2 times 5 kΩ) are still acceptable, since the input impedance of the differential amplifiers used is much higher (2 times 27 MΩ).

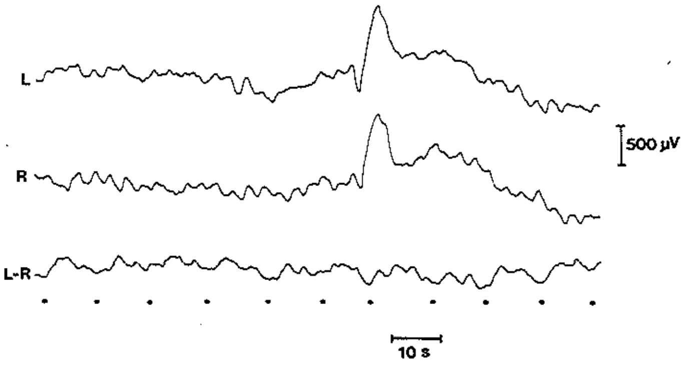

Fig.45 Characteristic relations between unipolar and bipolar abdominal signals (dog). L and R are unipolar signals, recorded with respect to the right hind leg. L - R is the bipolar signal (the difference between L and R).
Only in L - R the periodicity of the gastric component, indicated with dots, can be recognized. Most of the artifacts present in L and R are absent in L - R. The large deflection in L and R (absent in L - R) is probably due to a movement of the right hind leg, to which the reference electrode was attached.

Bipolar abdominal leads were found to yield the signals with the highest signal-to-noise ratio. A disadvantage of the use of any bipolar recording technique, however, is that it cannot be concluded from a bipolar signal which potential variations occurred at which electrode. This disadvantage is of no importance when only the repetition frequency of the signal is to be determined, but it counts heavily when the configuration of the signal is to be analyzed.
It was decided therefore, that in most of our studies, not only bipolar abdominal, but also unipolar abdominal leads would be used.

In the filtering of electrogastrographic signals it is essential that the fundamental gastric frequency (0.05 Hz in man, 0.08 Hz in the dog), is minimally attenuated.
When a 0.05 Hz sine wave is passed through a high-pass filter with a time constant of 3 s, its amplitude decreases by 37%. Nevertheless, time constants of 3 s and shorter have been used for electrograstrography in man (Tiemann and Reichertz, 1959a, 1959b; Martin et al., 1967; Martin et al., 1970; Martin and Thillier, 1971a; Sobakin et al., 1962; Sobakin and Privalov, 1976; Colombo et al., 1978). DC-coupling has been used by some investigators (Ingram and Richards, 1953; Davis et al., 1957; Russell and Stern, 1967; probably Stevens and Worrall, 1974), but is highly unpractical.
For our electrogastrographic studies a bandwidth of 0.012 to 0.46 Hz was chosen.

5.4 WHAT IS MEASURED IN ELECTROGASTROGRAPHY? (Dig.Dis.Sci., in press, 1980)

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5.4.1 Abstract

The object of this study was to elucidate what is actually measured in electrogastrography. Comparison of gastric signals simultaneously recorded from serosal and cutaneous electrodes in the conscious dog led to the following findings:

1. In the absence of phasic contractile activity and electrical response activity (ERA) the cutaneous recordings contained a frequency corresponding to the fundamental frequency of the electrical control activity (ECA) of the stomach (about 0.08 Hz).
2. Tachygastrias gave rise to cutaneous signals containing the tachygastric frequency (about 0.25 Hz).
3. The amplitude of the electrogastrogram increased when ERA occurred.

It is concluded that both ECA and ERA are reflected in the electrogastrogram. A model is proposed that describes the electrogastrogram as the result of field potentials generated by depolarization and repolarization dipoles.

5.4.2 Introduction

Electrogastrography (EGG) is the name given to the recording of gastric electrical activity from cutaneous electrodes. (In analogy with terms like electrocardiography and electroencephalography, it seems wise to reserve the term EGG for cutaneous recording and to renounce its use for intraluminal and serosal recording of gastric potentials.)
Since 1922[1] a limited number of investigators have published studies on EGG, mostly in man. Agreement exists on the sinuoidal configuration of the EGG signal and on its frequency in man, about 3 cycles per minute (0.05 Hz). The gastric origin of the signal was proven or claimed to be proven by several authors[1-6], but convincing evidence was provided only recently by Brown et al.[7] and Smallwood[8].
A question of major importance which has not yet been answered satisfactorily, is what exactly is measured in EGG. Most earlier investigators concluded or assumed that the electrogastrogram reflects the phasic contractile activity of the stomach. Due to a lack of knowledge of gastric myoelectric activity, the mechanism by which this reflection

is achieved could not be elucidated. It has been suggested that contraction-induced changes in the electrical impedance of the abdomen play a role in the generation of the electrogastrogram[9].
Studies made during the past 15 years yielded much information about the electrical activity of gastric smooth muscle. It is now known that in the extracellular signal derived with serosal electrodes two kinds of electrical activity can be distinguished. The first kind, often referred to as electrical control activity (ECA), is an omnipresent periodical activity that is not indicative of contractile activity. The second kind, the so-called electrical response activity (ERA), is time-locked to the ECA, but only occurs in connection with phasic contractile activity. Brown et al.[7] concluded from their experiments in man that gastric ECA is the only source of the electrogastrographic signal. This conclusion is in contrast with the assumption that in electrogastrography phasic contractile activity is measured.
The possibility that gastric ERA contributes to the surface signal has not yet been suggested as such in literature.

The object of this study was to identify the source(s) of the electrogastrogram. The principal method used to achieve this goal was the comparison of the electrical signals simultaneously derived from the gastric wall and the skin of the conscious dog.

5.4.3 Materials and methods

Four healthy dogs (Beagles) weighing between 10 and 14 kg, were used. Four bipolar electrodes were sutured to the serosal surface of the stomach (Fig.1A) under general anesthesia (induction with thiopental sodium, maintenance with nitrous oxide and enflurane) and using a sterile operating technique. In dogs 1, 3 and 4 two extraluminal strain-gauge transducers were placed in a transverse direction opposite electrodes 2 and 4. The serosal electrodes consisted of two silver/silver-chloride conical tips, 3 mm long, base diameter 0.2 mm, mounted 2 mm apart in a small plate. The electrode wires were connected to a 6-channel radio transmitter[10] implanted subcutaneously (dog 2), or to a multipin connector implanted in the animal's neck. For cutaneous recording disposable silver/silver-chloride ECG electrodes (14245A, Hewlett Packard) were used. Before placement of these electrodes some electrolyte paste (Redux Paste, Hewlett Packard) was rubbed on the shaved skin. Two electrodes were placed on the abdominal skin at sites selected in preliminary experiments (Fig.1B).
Recordings were made in the conscious state, starting one week after operation. On each dog weekly recording sessions, lasting from 1 to 16 hours, were carried out for at least 2 months. During recording sessions the dogs lay unrestrained in a measuring cage similar to their normal housing.
Recordings were made both in the fasting and in the postprandial state. When not subjected to fasting, the dogs were fed ad libitum with a dry food (Canex).
Recordings were made on curvilinear pen recorders (Van Gogh EP-8B) and on magnetic tape (Racal Store 14). In the bipolar serosal recordings connections were such that an upward deflection indicated that the proximal electrode was positive with respect to the distal and, in the cutaneous recordings, that the right abdominal electrode was positive with respect to the left one. The recordings of the bipolar serosal signals were made with cutoff frequencies of high- and low-pass filters (6 dB/oct) at 0.5 and 15 Hz respectively. For cutaneous recordings the

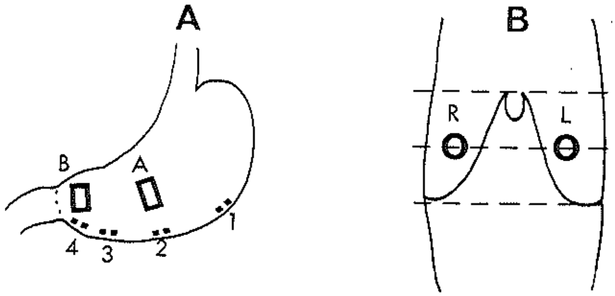

Fig.1 Positions of serosal and cutaneous electrodes and force transducers.

A. Bipolar serosal electrodes 1, 2, 3 and 4 placed along the greater curvature at 12, 7, 4 and 2 cm from the pylorus, respectively. Force transducers A and B opposite electrodes 2 and 4.

B. Abdominal surface electrodes R and L were placed 8 cm apart on a transverse line midway between the lower end of the body of the sternum and the lowest point of the costal arch.

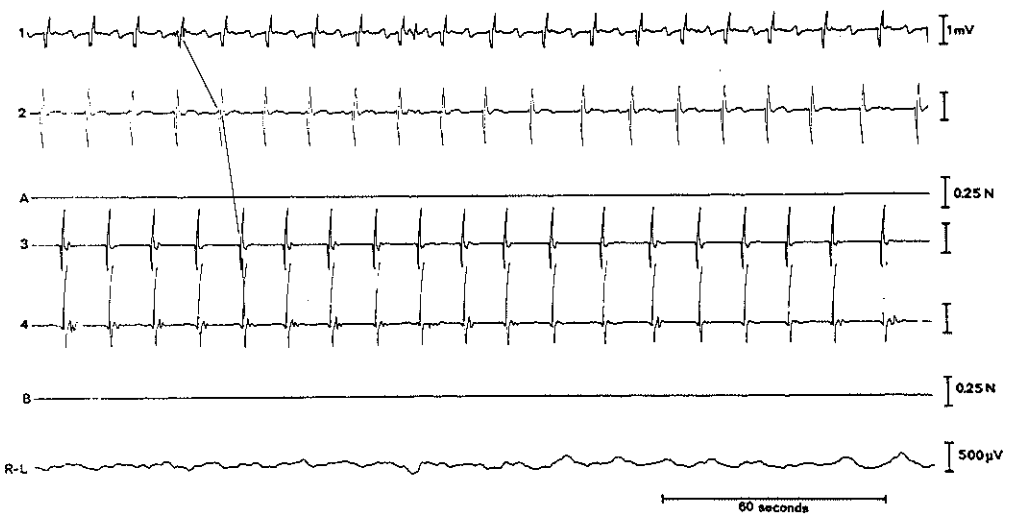

Fig.2 Recording of gastric myoelectrical and mechanical activity (bipolar serosal electrodes 1, 2, 3 and 4, strain-gages A and B) and the corresponding cutaneous signal (R - L).
Motor quiescence phase.

filters were set at 0.012 and 0.46 Hz. These latter filter settings were chosen for adequate elimination of base-line shifts and electrocardiogram. In addition to the bipolar serosal recordings, unipolar serosal recordings were made in dogs 3 and 4. The reference electrode (14245A, Hewlett Packard) was placed on the right hind leg. The records were divided into blocks of 1024 s (17.07 min.) duration and analyzed by means of visual examination and by means of Fast Fourier Transform, using a NOVA-2 minicomputer.

5.4.4 Results

In total 530 blocks of 17.07 min. were recorded. In 22 of these (4.2%) the cutaneous signal contained so much noise (mainly motion artifacts) that analysis was impossible.

Fig.2 illustrates the types of signals obtained from serosal electrodes, force transducers and cutaneous electrodes during absence of ERA (as in the motor quiescence phase of the interdigestive myoelectric complex[11]). In the cutaneous signal a small sinusoidal component of about 5 cycles per minute can be seen. This component was present in 91.4% of the blocks with complete motor quiescence. By means of spectral analysis it was demontrated that the fundamental frequency of this component and the fundamental frequency of the simultaneously derived serosal signal were always equal, which proved the gastric origin of the electrogastrogram (Fig.3). When a tachygastria[12] was present in the antrum, and ERA was absent, the cutaneous signal contained the tachygastric frequency (Fig. 4). From these results we conclude that gastric ECA contributes to the electrogastrogram.

When phasic contractions and ERA occurred, the amplitude of the electrogastrographic signal increased. As illustrated in Figs.5 and 6A, the amplitude variations of the cutaneous signal often ran parallel to the amplitude variations of the 'second potential'[13] derived from the distal antrum. (It should be noted here that in the canine stomach ERA does not always consist of spikes; often only second potentials are present. In this paper both second potentials without and second potentials with spikes are designated ERA.) However, as illustrated in Fig.6B, it was not possible to specify an EGG amplitude level above which contractions were always present, and below which there were never contractions. At this stage we had to conclude that the electrical phenomena that accompany the phasic contractions, or the phasic contractions themselves also contribute to the electrogastrogram.

In order to rule out the possibility that changes in the electrical impedance of the body, caused by gastric mechanical activity, play a role in the genesis of the electrogastrogram, the impedance variations of the tissue between the abdominal surface electrodes were recorded in two dogs. A 10 µA current at 1000 Hz was used, because at this frequency the impedance of the electrode-electrolyte interface is low in comparison with the impedance of the body[14]. The impedance records did not show any fluctuations corresponding to gastric contractions.The possibility that gastric contractions mechanically disturb the electrode-electrolyte interface and thus produce measurable potential variations can be ruled out by the simple observation that contractions of the stomach produced no visible movements of the surface electrodes, while relatively vigorous manipulation of the (recessed-type) electrodes produced no artifacts.

We conclude from the above that the electrogastrogram is generated by the myoelectric activity of the stomach and that both ECA and ERA are reflected in it.

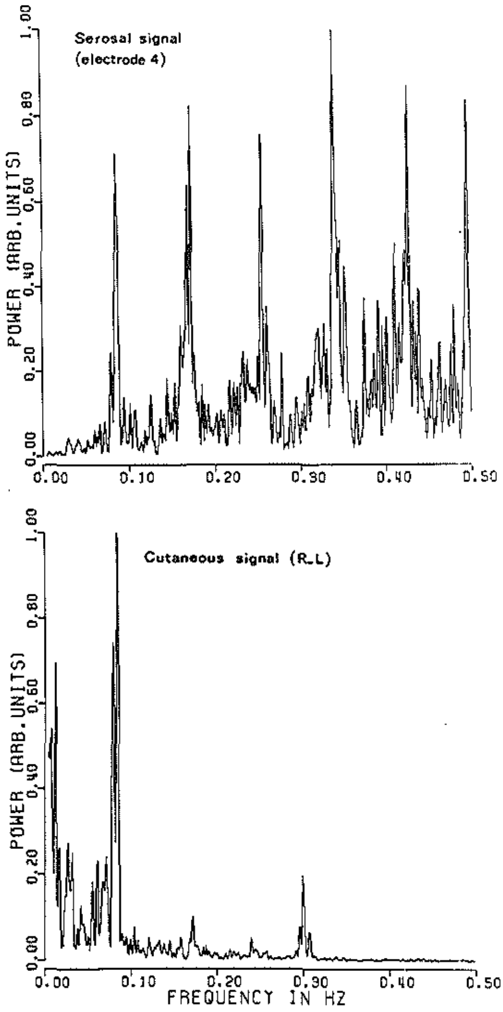

Fig.3 *Smoothed power spectra of signals simultaneously derived from serosal electrode 4 (upper spectrum) and cutaneous electrodes (lower spectrum). The duration of the analyzed stretch, part of which is shown in Fig.2, was 17.07 minutes. The peak at 0.30 Hz in the lower spectrum is probably of duodenal origin. The very low frequency peaks in the lower spectrum are in part due to noise originating in the electrode-skin interface and in part of unknown origin.*
Motor quiescence phase.

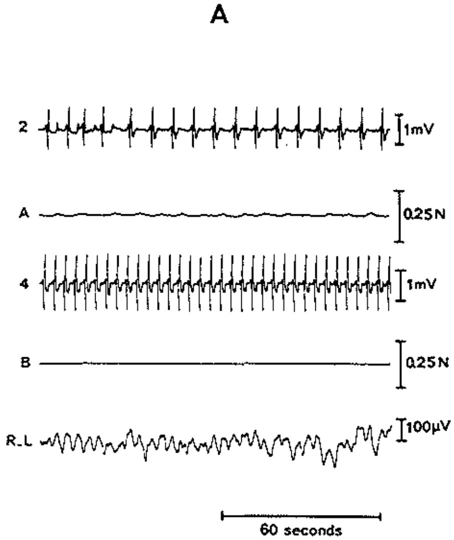

Fig.4A Tachygastria recorded from serosal (2 and 4) and cutaneous (R-L) electrodes.

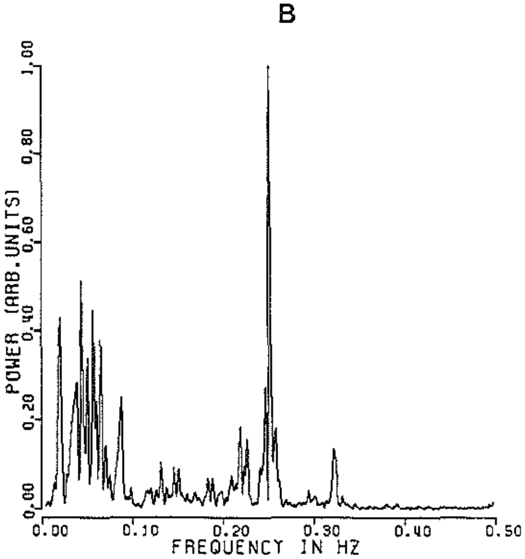

Fig.4B Smoothed power spectrum of the cutaneous signal shown in A. The frequency of the tachygastria is 0.25 Hz.

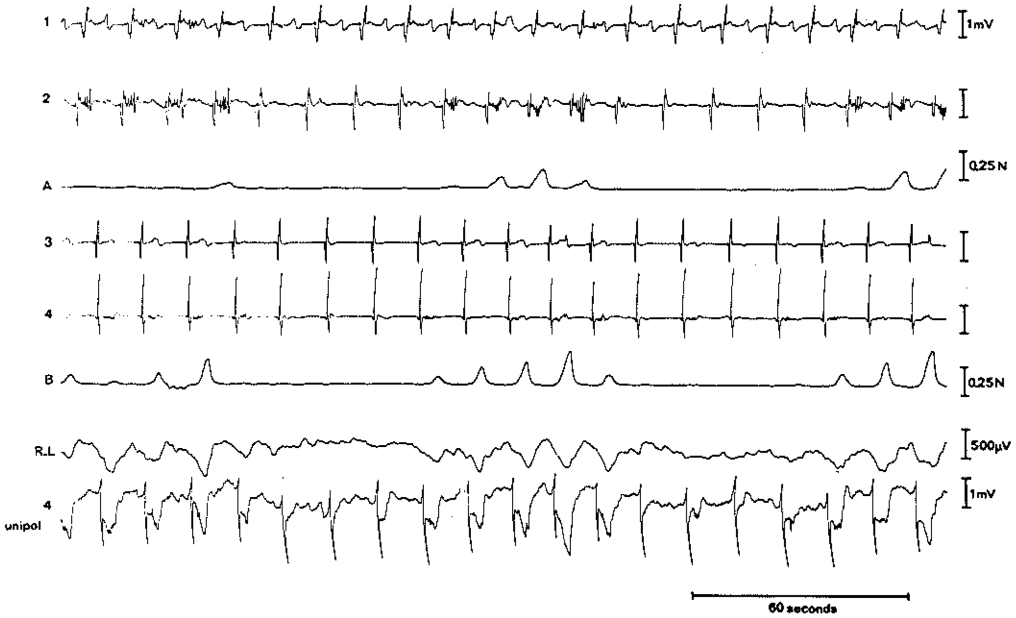

Fig.5 Recording of gastric myoelectrical and mechanical activity (bipolar serosal electrodes 1, 2, 3 and 4, strain gages A and B) and the corresponding cutaneous signal (R-L). The bottom signal was derived from electrode 4 by means of a unipolar technique (filter settings 0.025 and 15 Hz). In this signal the second potential is more easily recognized than in the bipolar signals.

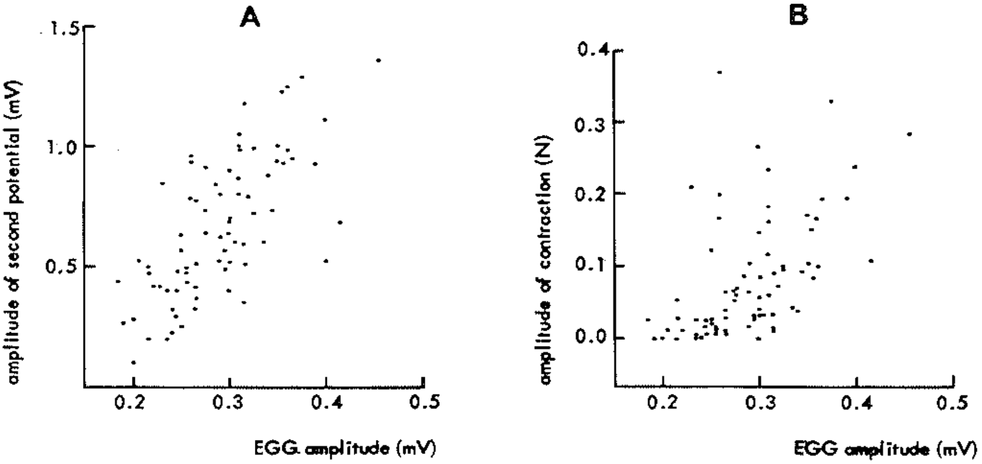

Fig.6 Example of the relation between EGG amplitude and amplitude of the second potential (A) and of the relation between EGG amplitude and contractile force(B). Amplitude of second potential and contractile force were measured from signals obtained with electrode 4 (unipolar) and force transducer B, respectively. The figure covers

80 consecutive ECA intervals (one 17.07 min. block). Fasting dog, intermediate type of motor pattern.

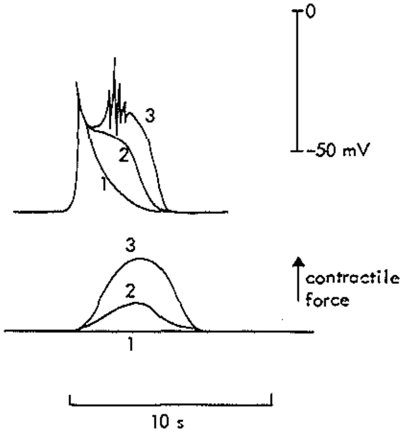

Fig.7 Intracellularly recorded electrical activity of antral smooth muscle and the corresponding mechanical activity. Stronger contractions are related to higher plateaus of longer duration. The spikes shown here on the plateau may be absent (after Daniel[13]; Papasova et al.[15] and Szurszewski[16]).

4.4.5 Discussion

The finding that the gastric frequency can be derived from the skin in the absence of phasic contractile activity is in accordance with the results of Brown et al.[7], who concluded from their experiments in man that in EGG the basic electrical rhythm (i.e. ECA) of the stomach is measured.

However, our study shows that not only ECA, but also ERA is reflected in the electrogastrogram. In order to explain the increased amplitudes of electrogastrograms after a meal, Brown and colleagues supposed that after a meal the closer proximity of the electrodes to the distended stomach accounts for better recording conditions. Although it seems likely that variations in the position of the stomach modulate the amplitude of the electrogastrogram, this mechanism cannot be the only one involved, since we also observed increased amplitudes during isolated contractions in an empty stomach (during IDMEC phase II[11]).

Our conclusion that both ECA and ERA are reflected in the electrogastrogram explains the correlation between phasic contractions of the stomach and increased amplitudes in the electrogastrogram, as observed or postulated by most investigators in this field.

In order to obtain a better insight into the genesis of the electrogastrographic signal, dipole theory was applied to gastric electrical activity. The following description of the resulting provisional EGG model will be in qualitative terms; for a quantitative and mathematical treatment the reader is referred to the Appendix.

It is known from work with intracellular electrodes[13,15] and with the sucrose-gap technique[16] that in antral smooth muscle there is a fast initial depolarization followed by a plateau. Spikes may occur superimposed upon the plateau. The duration and amplitude of the plateau increase with increasing contractile force, while the configuration of the initial depolarization is relatively constant (Fig.7). The initial depolarization gives rise to an ECA pulse in the extracellular recording. Spikes and repolarization manifest themselves in the extracellular recording as spikes and second potential, respectively.

In the present model initial depolarization and repolarization are represented as dipoles. The depolarization dipoles are considered to be of constant magnitude, while the magnitudes of the repolarization dipoles vary with repolarization rate. The spikes, being asynchronous oscillations of the membrane potentials of individual cells, are assumed not to constitute significant dipoles.

During motor quiescence the plateau is small or absent and the rate of repolarization is low. Therefore, repolarization dipoles are thought to be absent or of low amplitude during motor quiescence; only depolarization dipoles are present. At some distance from the stomach, the slowly propagating series of depolarization dipoles is recorded as a sinusoidal signal (Fig.8A).

When contractions occur and repolarization rates are higher, repolarization dipoles are present between the depolarization dipoles. Since these give rise to potentials of opposite polarity with a phase difference of about π radians with the depolarization effects, the summation of the potentials generated by both types of dipoles yields a sinusoidal signal of increased amplitude (Fig.8B).

Although the above described model is only a first approximation, the sinusoidal configuration of the electrogastrographic signal as well as the ERA-related amplitude changes can be understood with it.

Much more work has to be done before the electrogastrogram can be understood to the full. For instance, our data suggest that the activity of the distal antrum dominates the electrogastrogram. This could be explained by the fact that both amplitude and propagation velocity of gastric myoelectric activity increase towards the pylorus. It should be investigated, however, whether electrodes at other sites on the abdomen 'see' other parts of the stomach.

Whether the electrogastrogram might eventually be used as a diagnostic tool, as has already been claimed by several authors[3,6,17-20], is a question that cannot be answered on the basis of the present study.

5.4.6 Appendix

In a volume conductor the potentials generated by bioelectric events can be described with the aid of dipoles. In the presented EGG model current dipoles were used, each consisting of a source of current I and nearby sink of current I.

A current point source in a homogeneous, conducting medium produces a potential field ϕ_p in a point P:

$$\phi_p(r) = \frac{I}{4\pi\sigma} \cdot \frac{1}{r}$$

where r = the distance from P to the source
and σ = the conductivity of the medium.

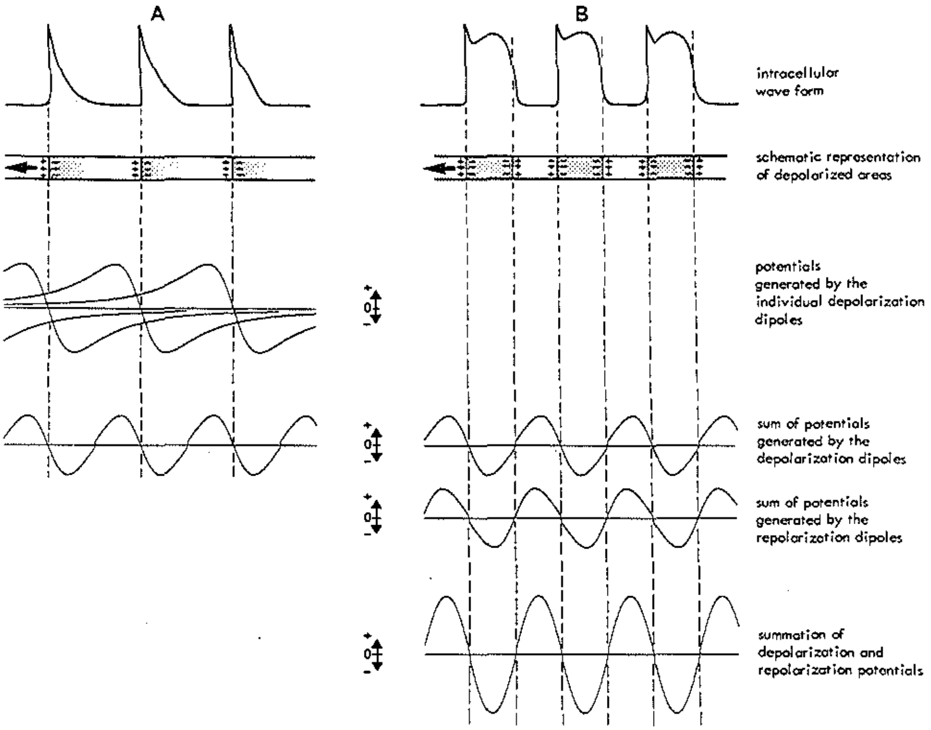

Fig.8A *Computer simulation of the potential variations recorded when a series of equally spaced depolarization dipoles travels slowly underneath a remote electrode, as in a mechanically inactive stomach.*

Fig.8B *Computed potential variations when in addition to depolarization dipoles repolarization dipoles are present, as in mechanically active stomach.*
(Distance from electrode to dipole axis 5 cm. For other parameters see Appendix.)

The potential at a point P at (x,y) produced by a source and a sink on the x-axis at (-b,0) and (b,0) is

$$\phi_p(x,y) = \frac{I}{4\pi\sigma}\left(\frac{1}{\sqrt{(x+b)^2+y^2}} - \frac{1}{\sqrt{(x-b)^2+y^2}}\right).$$

Both depolarization and repolarization propagating along a nerve fibre or a muscle cell can be represented by a travelling current dipole. The magnitudes of sources and sinks and the source-sink distances depend on the intracellular wave form, since it can be shown that the current through the membrane is proportional to the second derivative of the membrane potential[14]. Taking the proportionality factor 1, depolarization and repolarization can each be represented by a current dipole

$$i_m = h\delta(x+b) - h\delta(x-b),$$

where i_m = the current through the membrane,
h = the slope of the membrane potential change, and
δ = the Dirac delta function,

as illustrated in Fig.A-1.
The magnitude I of source and sink is proportional to h and the distance between source and sink amounts 2b.
When the membrane potential is constant, no dipoles are present and no external field exists. All propagating membrane activities can be described either as time- or as place-dependent changes, these being related through the velocity v (= dx/dt) of the propagating phenomenon.

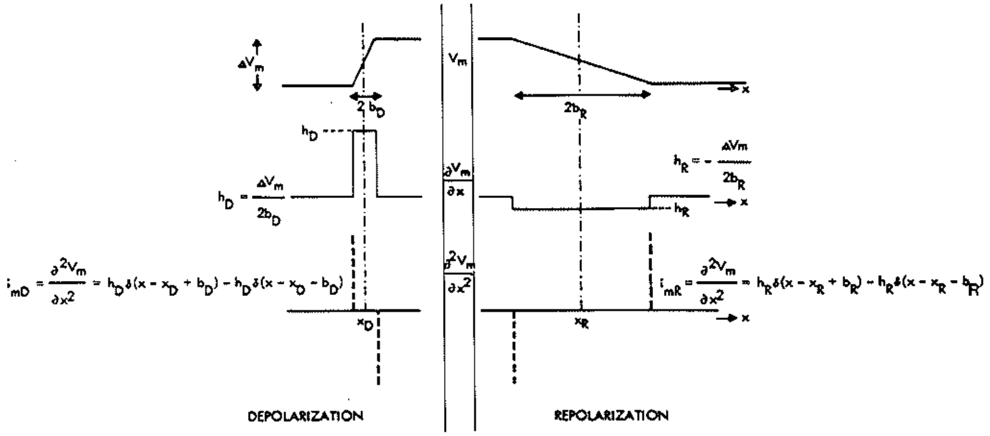

Fig.A-1 Construction of depolarization and repolarization dipoles from a schematic intracellular waveform.
V_m is the membrane potential, for further explanation see text.

Fig.A-2 shows the potential distribution along a line parallel to the x-axis generated by one stationary dipole on the x-axis. If the dipole is assumed to travel along the x-axis, Fig.A-2 shows the potential variations at a fixed point and the abscissa has the dimension of time.

In the EGG model presented in this paper the following assumptions were made:
- the stomach is a cylinder of infinite length,
- the cylinder is homogeneously filled with muscle cells,
- both depolarization and repolarization take place synchroneously in the radial plane,
- depolarization and repolarization fronts are propagated with constant velocity.

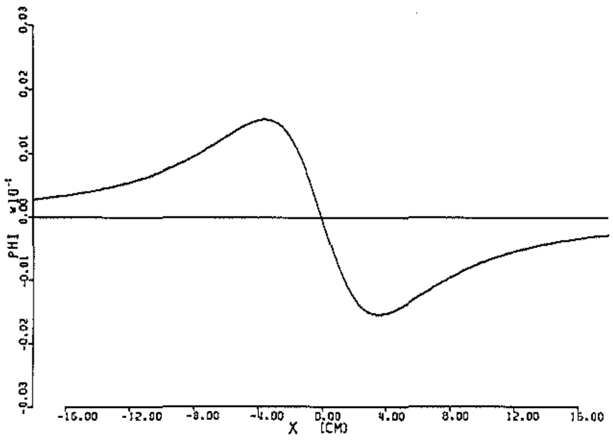

Fig.A-2 Potential ϕ at a line parallel to the x-axis ($y = 5$ cm) generated by a stationary current dipole with source at $(-b,0)$ and sink at $(b,0)$ ($b = 0.05$ cm).
Ordinate: potential ϕ in units $I/4\pi\sigma$.

It was further approximated that:

- all dipoles in a radial plane are located at the cylinder axis. It can be shown that this leads to errors smaller than 1% when the distance to the cylinder axis is more than twice the cylinder radius. Consequently, one of the features of the model is that ring-shaped deformations of the stomach (phasic contractions) hardly influence the potential field at some distance from the cylinder.

With regard to the repolarization dipoles the following approximations were made:

- in the absence of contractions the magnitude of the repolarization dipole is zero, since the slope of repolarization is relatively small (see Fig.7, curve 1).
- in the presence of strong contractions the repolarization dipole is as strong as the depolarization dipole (but of opposite polarity), since in that case the slope of repolarization is almost as steep as the depolarization slope (Fig.7, curve 3).

With these approximations and assumptions the potential at a point P(x,y) generated by one depolarization and one repolarization front propagating over the stomach is:

$$\phi_P(x,y) = \frac{1}{4\pi\sigma}\left\{ I\left(\frac{1}{\sqrt{(x-x_D+b)^2+y^2}} - \frac{1}{\sqrt{(x-x_D-b)^2+y^2}}\right) + \right.$$

$$\left. - \alpha I\left(\frac{1}{\sqrt{(x-x_R+b)^2+y^2}} - \frac{1}{\sqrt{(x-x_R-b)^2+y^2}}\right)\right\}$$

where $(x_D,0)$ = the center of the depolarization dipole,

$(x_R,0)$ = the center of the repolarization dipole,

$\alpha = 0$ for absence of phasic contractions

$\alpha = 1$ for presence of strong phasic contractions.

The results of the model for a series of consecutive depolarization and repolarization dipoles are shown in Fig.8.
For the propagation velocity of the dipoles 1 cm/s was chosen and for the time interval between the depolarization dipoles 12.5 s. The resulting distances between consecutive depolarization dipoles is 12.5 cm. Based on an approximated slope of depolarization of 1 V/cm and a membrane potential change of 100 mV, the distance between source and sink of one dipole was fixed at 0.1 cm.

5.4.7 References

1. Alvarez, W.C.
"The electrogastrogram and what it shows"
J.Am.Med.Ass. 78; 1116-1119, 1922

2. Davis, R.C., Garafolo, L., Gault, F.P.
"An exploration of abdominal potentials"
J.Comp.Physiol.Psychol. 52; 519-523, 1957

3. Nelsen, T.S., Kohatsu, S.
"Clinical electrogastrography and its relation to gastric surgery"
Am.J.Surg. 116; 215-221, 1968

4. Martin, A., Moline, J., Thouvenot, J.
"Potentiels électriques dérivés à la surface de l'abdomen en relation avec l'activité antropylorique chez l'animal et chez l'homme"
C.R.Soc.Biol. (Paris) 163; 1423-1425, 1969

5. Drieux, C., Garnier, D., Martin, A., Moline, J.
"Corrélation entre l'activité électrique de l'antre gastrique et l'électrogastro-entérogramme du Cobaye.
J.Physiol. (Paris) 73; A20, 1977

6. Tonkovic, S., Thouvenot, J., Penaud, J.
"Electrosplanchnographical exploration of the digestive tract diseases.
Digest 11th International Conference on Medical and Biological Engineering, Ottawa, 1976

7. Brown, B.H., Smallwood, R.H., Duthie, H.L., Stoddard, C.J.
"Intestinal smooth muscle electrical potentials recorded from surface electrodes.
Med.Biol.Eng. 13; 97-103, 1975

8. Smallwood, R.H.,
"Gastrointestinal electrical activity from surface electrodes"
Thesis, Sheffield, 1976

9. Thouvenot, J., Penaud, J., Morelle, O.
"Sur les phénomènes électrophysiologiques des viscères: leur traduction à la surface cutanée"
J.Phyriol. (Paris) 65; A170-171, 1972

10. Besseling, N.C., Van Maaren, D.Ch., Kingma, Y.J.
"An implantable biotelemetry transmitter for six differential signals"
Med.Biol.Eng. 14; 660-664, 1976

11. Code, C.F., Marlett, J.A.
"The interdigestive myoelectric complex of the stomach and small bowel of dogs"
J.Physiol. (London) 246; 289-309, 1975

12. Code, C.F., Marlett, J.A.
"Canine tachygastria"
Mayo Clin.Proc. 49; 325-332, 1974

13. Daniel, E.E.,
"The electrical and contractile activity of the pyloric region in dogs and the effects of drugs"
Gastroenterology 49; 403-418, 1965

14. Geddes, L.A.
"Electrodes and the measurement of bioelectric events"
New York, Wiley-Interscience, 1972

15. Papasova, M.P., Nagai, T., Prosser, C.L.
"Two-component slow waves in smooth muscle of cat stomach"
Am.J.Physiol. 214; 695-702, 1968

16. Szurszewski, J.H.
"Mechanism of action of pentagastrin and acetylcholine on the longitudinal muscle of the canine antrum"
J.Physiol. (London) 252; 335-361, 1975

17. Tiemann, F., Reichertz, P.
"Über das intestinale Elektrogramm (E.I.G.) und seine Bedeutung für die Klinik"
Med.Klin. 14; 654-668, 1959

18. Sobakin, M.A., Smirnov, I.P., Mishin, L.N.
"Electrogastrography"
IRE Trans.Bio.Med.Electron. 9; 129-132, 1962

19. Martin, A., Moline, J., Murat, J.
"Apport de l'électrosplanchnographie (E.S.G.) au diagnostic pré-opération d'une ulcération gastrique"
Presse Médical 28; 1277-1278, 1971

20. Martin, A., Thillier, J.L., Moline, J.
"Effets de la section du vague sur la motricité gastrique chez l'homme. Etude électrogastro-entérographique"
J.Physiol. (Paris) 65; A145, 1972.

Acknowledgements

The authors gratefully acknowledge the technical assistance of Mr. J.V. de Bakker and Mr. W.H. Groeneveld and wish to thank Mr. M.A. Kentie for his constructive suggestions.
The animal experiments described in this paper were carried out in co-operation with the Laboratory for Experimental Surgery of the Erasmus University Rotterdam, which is under the direction of Dr. D.L. Westbroek.

Proceedings of the 7th International Symposium on Gastrointestinal Motility, held at Iowa City, Iowa, September 1979. Raven Press, in press, 1979.

5.5 POSTPRANDIAL AND INTERDIGESTIVE GASTRIC ELECTRICAL ACTIVITY IN THE DOG RECORDED BY MEANS OF CUTANEOUS ELECTRODES

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5.5.1 Introduction

From the skin, potential variations can be recorded that are generated by the stomach. This method can be designated Electrogastrography (EGG).
As described already by Alvarez in 1922 (1), the electrogastrographical signal is sinusoidal and has a frequency equal to the repetition frequency of phasic gastric activity (in man 3 cycles per minute, in the dog 5 cpm).
However, what exactly is measured in EGG has long remained unclear. Most authors concluded or assumed that the electrogastrogram reflects the phasic contractile activity of the stomach. In contrast, Brown et al. (2) concluded from a study in man that in EGG gastric electrical control activity (ECA) is measured.
From a recent study in the dog we concluded that the electrogastrogram reflects both electrical control activity and electrical response activity (ERA) of the stomach. When only ECA is present, and thus contractile activity is absent, the amplitude of the electrogastrographic sinusoid is small. The amplitude increases when in addition to ECA ERA occurs, but the relation between EGG amplitude and contractile force, as measured with extraluminal force transducers, is not very strong.
The digestive and interdigestive patterns of canine myoelectric and contractile activity have recently been the subject of extensive studies using serosal electrodes and extraluminal force transducers. In the fasted state the motor pattern of stomach and small bowel is reported to consist of a cyclic recurrence of episodes of strong contractions, alternating with episodes of complete motor quiescence (6, 7). The electric correlate of this pattern, which migrates along the small intestine, has been designated 'migrating (myo)electric complex' (11) and 'interdigestive myoelectric complex' (4); terms abbreviated in the literature to MMC and IDMEC. When both motor and myoelectrical activity are studied, the term 'interdigestive migrating complex' (IMC) is to be preferred.
The digestive or postprandial pattern consists of a steady contractile activity of moderate intensity (6), or, when studied with serosal electrodes of the presence of moderate ERA with each electrical control potential (4).

The object of this study was to describe the characteristics of the cutaneous (electrogastrographic) signal in relation to the digestive and interdigestive patterns in the canine stomach.

5.5.2 Methods

Four healthy dogs (Beagles) were used. Four bipolar electrodes and (in three of the dogs) two strain-gauge force transducers were sutured to the serosal surface of the stomach, at the sites shown in Fig.1A. In one of the dogs an additional bipolar electrode was implanted on the serosal surface of the duodenum, at a distance of 3 cm from the pylorus.

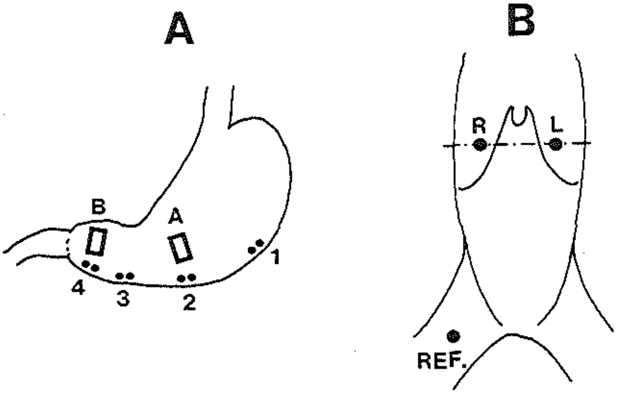

Fig.1.A Bipolar serosal electrodes 1, 2, 3 and 4 at 12, 7, 4 and 2 cm from the pylorus, respectively. Strain-gauge force transducers A and B placed in transverse direction opposite electrodes 2 and 4.

B Abdominal surface electrodes R and L 8 cm apart on a transverse line midway between the lower end of the body of the sternum and the lowest point of the costal arch, and reference electrode on right hind leg.

Recordings were made with conscious dogs, starting one week after operation. Before each recording session two disposable ECG electrodes (14245A, Hewlett Packard) were placed on the shaved skin of the abdomen, at the sites shown in Fig.1.B. A third (reference) electrode was placed on the right hind leg. The potential difference between the two abdominal electrodes as well as between each of the abdominal electrodes and the leg electrode were recorded. In this paper only the bipolar cutaneous signal (R-L) will be considered, since this contained the fewest motion artifacts.
Recordings were made on paper (Van Gogh EP-8b) as well as on magnetic tape (Racal Store 14). For serosal electrical signals the high- and lowpass filters (6 dB/oct) were set at 0.5 and 15 Hz respectively, for cutaneous signals at 0.012 and 0.46 Hz.
With each dog weekly recording sessions, lasting from 1 to 16 hours, were carried out for at least two months. Recordings were made both in

the interdigestive state (after more than 20 hours fasting) and in the postprandial state.
Besides visual examination of the original chart recordings the following methods were used in the analysis of the cutaneous signals:

- additional band-pass or low-pass filtering, using Krohn-Hite 3322 filters (Butterworth, 24 dB/oct)
- spectral analysis of stretches of 1024 s (17.07 min.) duration, using a Fast Fourier Transform algorithm and a NOVA-2 computer.

5.5.3 Results

General Observations

In the stomach of our fasted dogs an interdigestive migrating complex (IMC) was not always present. One of the dogs, although in good health, never showed gastric IMC. In the fasted state the stomach of this dog usually showed a contractile pattern best described as quiescent periods of a few minutes interrupted by a few consecutive contractions. This 'minute pattern' was observed in two of the other dogs as well (in about 30% of the fasted recordings).
The activity front of the IMC appeared to be characterized by the periodic occurrence of groups of strong contractions, rather than by a continuous succession of strong contractions as is the case in the small intestine.
Superimposed upon the gastric component of the cutaneous signal (frequency around 5 cpm) a component of around 19 cpm was often present, particularly in the fasted state. In the dog with the duodenal electrode the frequency of this latter component was found to be equal to the fundamental frequency of the duodenal ECA.

Characteristics of the Electrogastrographic Signal

Postprandial pattern

The postprandial cutaneous signal was characterized by a constant, high amplitude of the gastric component (Fig.2A). The amplitude was as high as, or even higher than, that during the strongest contractions of the activity front (up to 1 mV).

Interdigestive patterns

IMC. 40 IMC cycles were studied. In five of these analysis of the cutaneous signal was rendered impossible by artifacts (caused by body movements). In the remaining 35 cycles the cutaneous signal exhibited the characteristics to be described here.
During the phase of complete motor quiescence (phase I in the classification by Code and Marlett (4)) the amplitude of the (sinusoidal) gastric component of the cutaneous signal was small (Fig.2.B). In this phase spectral analysis or additional band-pass filtering was often required to demonstrate the presence of a gastric component.

In two dogs antral tachygastrias (3) occasionally occurred in phase I. During their presence a frequency equal to the fundamental frequency of the tachygastria was present in the cutaneous signal (Fig.3).

During the activity front of the IMC (phase III) periodic increases of the amplitude of the 0.085 Hz sinusoid were observed. These increases coincided with the occurrence of groups of strong contractions characteristic of this phase.

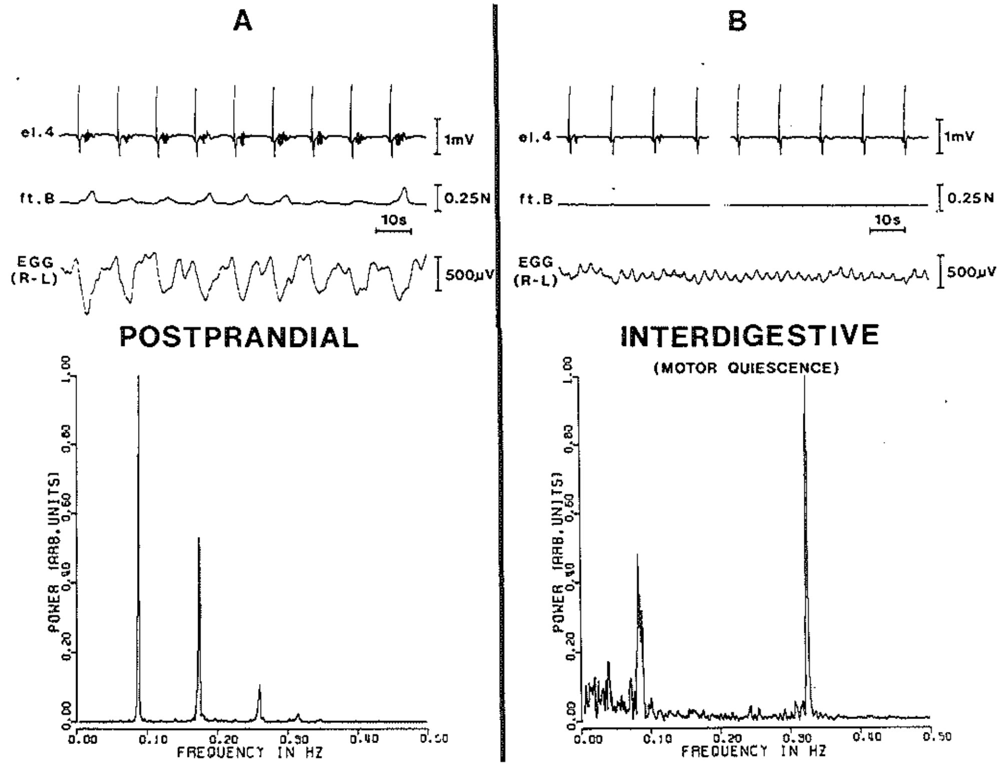

Fig.2 The electrogastrographical signal (R–L) and its normalized power spectrum during the postprandial (A) and interdigestive motor quiescence phase (B). el.4 and ft.B are the signals recorded from serosal electrode 4 and force transducer B.
In the postprandial spectrum a fundamental gastric peak at 0.086 Hz (5.16 cpm) is present, as well as two higher harmonics (at 0.171 and 0.257 Hz). The peak at 0.314 Hz (18.81 cpm) is of duodenal origin. Ordinate: 1 unit equals 1336 μV^2.
In the spectrum of the motor quiescence EGG the gastric peak is at 0.082 Hz (4.92 cpm) and the duodenal peak is at 0.324 Hz (19.45 cpm). Ordinate: 1 unit equals 380 μV^2.

The periodical occurrence of these groups of contractions was also accompanied with the presence of lower frequency components in the cutaneous signal (Fig.4).
Band-pass filtering of the cutaneous signal (letting through a narrow frequency band around 0.085 Hz) facilitated the recognition of the amplitude increases and ultra-low-pass filtering made the very low-frequency component visible (Fig.5).

'Minute pattern'. As mentioned, in the serosal recordings from three of the dogs an alternating pattern with a periodicity of 1 to 3 minutes was often observed instead of IMC. When this pattern was present, the cutaneous signal showed an amplitude modulation with this rhythm.

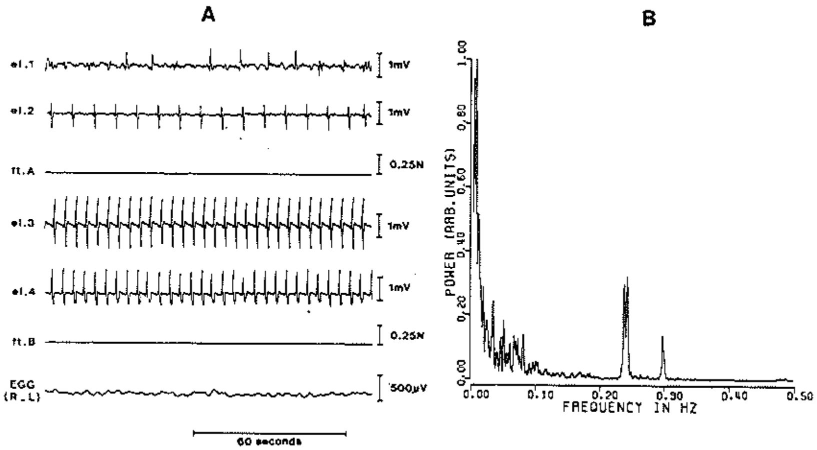

Fig.3 Regular antral tachygastria.

A. Serosal and cutaneous signals as function of time.
B. Normalized power spectrum of the cutaneous signal.

The frequency of the tachygastria is around 0.24 Hz (14.6 cpm). There is a duodenal peak at 0.298 Hz (17.87 cpm). Ordinate: 1 unit equals 68 µV^2.
As a consequence of the low signal-to-noise ratio of the cutaneous signal, the spectrum is dominated by low-frequency noise originating in the electrode-skin interface.

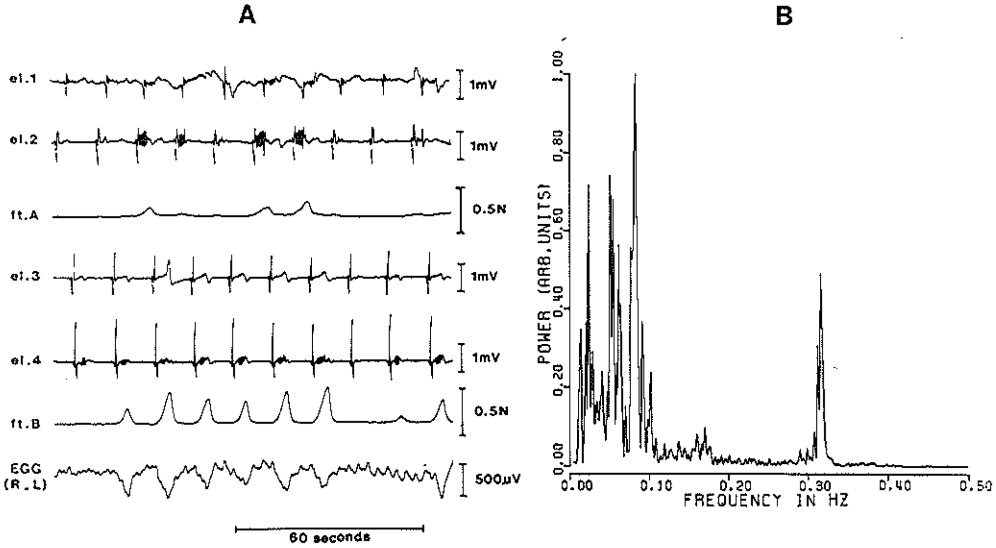

Fig.4 IMC phase III (activity front).

A. Signals as function of time.
B. Normalized power spectrum of the cutaneous signal.

The gastric frequency is 0.082 Hz (4.92 cpm). The duodenal frequency is 0.315 Hz (18.92 cpm). Ordinate: 1 unit equals 320 µV^2.

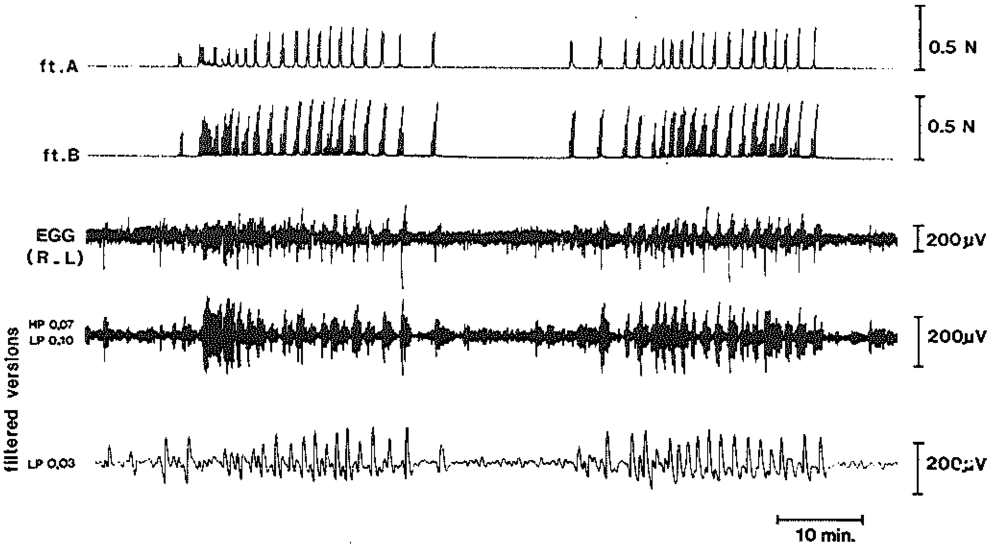

Fig.5 Gastric IMC and its recognition from the cutaneous signal. R-L is the raw cutaneous signal as recorded on tape. The upper filtered version shows the cutaneous signal after additional band-pass filtering. The lower filtered version shows the signal after ultra-low-pass filtering. Both in the band-passed and in the ultra-low-passed version the IMC can be recognized.

5.5.4 Discussion

In view of the literature on the interdigestive migrating complex the finding that an IMC was not consistently present in the stomach of our fasted dogs might be considered unusual. In an earlier study, however, we made the same observation (10). In this connection it is interesting to read the description of the fasted gastric motor pattern provided by Nelsen et al. (8) in 1966. This description completely covers the 'minute pattern' encountered in three of our fasted dogs.
This study shows that the IMC in the canine stomach, when present, can be detected with the completely non-invasive technique of EGG. In addition, the method permits the measurement of IMC parameters as IMC cycle duration and duration of the activity front.
The origin of the activity-front-related low-frequency components in the cutaneous signal was not investigated in this study. It seems possible however, that these low-frequency changes are related to the prolonged ECA intervals that have been shown to coincide with the strongest contractions of the activity front (5, 10).
It may be hoped that EGG can also be used for the study of gastric interdigestive patterns in man. However, it must be realized that the use of EGG for this purpose has some drawbacks. A first drawback is constituted by the fact that the electrogastrogram reflects the myoelectrical activity of the stomach and does not provide direct information regarding the strength of the contractile activity of the organ. A second drawback is that motion artifacts have about the same frequency content as the electrogastrogram and therefore seriously hamper its interpretation. Improvement of our understanding of the electrogastrographic signal and development of specialized recording and analyzing techniques is needed

before widespread (clinical) use of EGG for the study of the IMC can be advocated.

The above-mentioned drawbacks play a much smaller role in the electrogastrographic measurement of mean ECA frequencies (of both stomach and duodenum). In our two dogs in which tachygastrias occurred the electrogastrographic detection of the accelerated gastric rhythm appeared to be relatively easy. Whereas tachygastrias of short duration are probably physiological (3), prolonged tachygastrias must be considered pathological, since in the presence of a tachygastria the antrum is mechanically inactive. Very recently two patients have been described in which idiopathic gastric retention appeared to be accompanied by a tachygastria (9, 12), which was diagnosed with invasive techniques. In cases like these, EGG might well become an important diagnostic aid.

In conclusion, this study showed that the method of EGG provides information about the mean frequency of gastric (and duodenal) electrical control activity and, furthermore, provides information about the postprandial and interdigestive myoelectrical patterns in the stomach of the conscious dog.

5.5.5 References

(1) Alvarez, W.C. (1922)
J.A.M.A., 78; 1116-1119.

(2) Brown, B.H., Smallwood, R.H., Duthie, H.L. and Stoddard, C.J. (1975)
Med.Biol.Eng., 13; 97-103.

(3) Code, C.F. and Marlett, J.A. (1974)
Mayo Clin.Proc., 49; 325-332.

(4) Code, C.F. and Marlett, J.A. (1975)
J.Physiol. (London), 246; 289-309.

(5) Hiesinger, E., Hoernicke, H. and Ehrlein, H.J. (1977)
In: Gastrointestinal Motility in Health and Disease, edited by H.L. Duthie, pp 275-285. MTP Press, Lancaster, England.

(6) Itoh, Z., Aizawa, I., Takeuchi, S. and Takayanagi, R. (1977)
Am.J.Dig.Dis., 22; 117-124.

(7) Itoh, Z., Takeuchi, S., Aizawa, I. and Takayanagi, R. (1978)
Am.J.Dig.Dis., 23; 229-238.

(8) Nelsen, T.S., Eigenbrodt, E.H. and Keoshian, L.A. (1966).
Arch.Surg., 92; 279-385.

(9) Sanders, K., Menguy, R., Chey, W., You, C., Lee, K., Morgan, K., Kreulen, D., Schmalz, P., Muir, T. and Szurszewski, J. (1979).
Gastroenterology, 76; 1234.

(10) Smout, A.J.P.M., Van der Schee, E.J. and Grashuis, J.L. (1979)
Am.J.Physiol., 237; E279-E283.

(11) Szurszewski, J.H. (1969)
Am.J.Physiol. 217; 1757-1763.

(12) Telander, R.L., Morgan, K.G., Kreulen, D.L., Schmalz, P.F., Kelly, K.A. and Szurszewski, J.H. (1978).
Gastroenterology, 75; 497-501.

Acknowledgements

The animal experiments described in this paper were carried out at the Erasmus University Laboratory for Experimental Surgery, which is under the direction of Dr. D.L. Westbroek.
The authors wish to thank Mr. J.V. de Bakker and Mr. W.H. Groeneveld for their technical assistance.

5.6 *Electrogastrographic explorations in man*

5.6.1 *Introduction*

The object of our electrogastrographic explorations in man was to investigate the possibilities of recording electrogastrographic signals from the human skin and to describe some characteristics of these signals.

5.6.2 *Methods*

Both bipolar and unipolar abdominal signals were recorded in a series of 17 healthy volunteers (16 - 37 years of age).
The positions of the abdominal electrodes used in our human studies are shown in Fig.46.

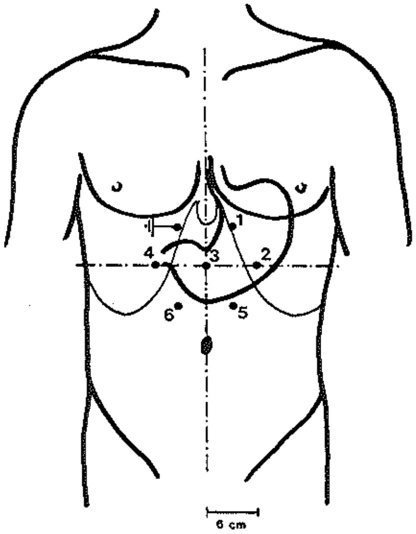

*Fig.46 Positions of abdominal electrodes used in our electrogastrographic studies in man.
The electrodes 2, 3 and 4 are situated on Addison's line; this is a transverse line halfway between the lower end of the sternum and the navel (transpyloric line). Electrode 3 is placed at the intersection of the line of Addison and the median plane. The distance between all other electrodes and electrode 3 is 6 cm. The seventh electrode depicted is an earth electrode.*

The indifferent electrode needed for unipolar recording was placed on the right leg, just above the ankle.
In practice, only the six unipolar signals (potential differences of the abdominal electrodes with respect to the reference electrode on the right ankle) were recorded on magnetic tape. All bipolar signals were obtained by means of electronic subtraction of unipolar signals.

After an overnight fast the electrodes (Hewlett Packard 14245A or Harco type 155) were attached to the skin. A strain-gauge force transducer was placed laterally on the lower part of the chest to record the respiratory movements.
From all subjects fasting activity was recorded during 35 minutes. Subsequently, a test meal, consisting of 250 ml of yoghurt with 20 g of sugar, was taken. Immediately after the test meal recording was resumed and continued for 55 minutes.
The subjects were requested to lie quietly during the entire recording session.

All bipolar and unipolar signals were analyzed by means of visual inspection.
Furthermore, Fourier analysis was applied to the bipolar signal 1 - 4. As in the dog, power spectra of successive signal stretches of 1024 s (17.07 min.) duration were calculated. Two fasting and three postprandial stretches of the 1 - 4 signal were analyzed in all subjects.

5.6.3 Results

5.6.3.1 Visual analysis

Fig.47 gives an example of the unipolar signals recorded before and after the test meal.
As a rule, a gastric component could hardly be recognized in the fasting unipolar signals. In the postprandial phase, however, a sinusoidal periodical component (frequency about 0.05 Hz or 3 cpm) was always seen in at least one of the unipolar signals. In Fig.47 the gastric component is seen most clearly in the postprandial signals 1, 2 and 3. In these signals the gastric waves are approximately in phase. The higher frequency component present in most of the signals is respiration artifact.

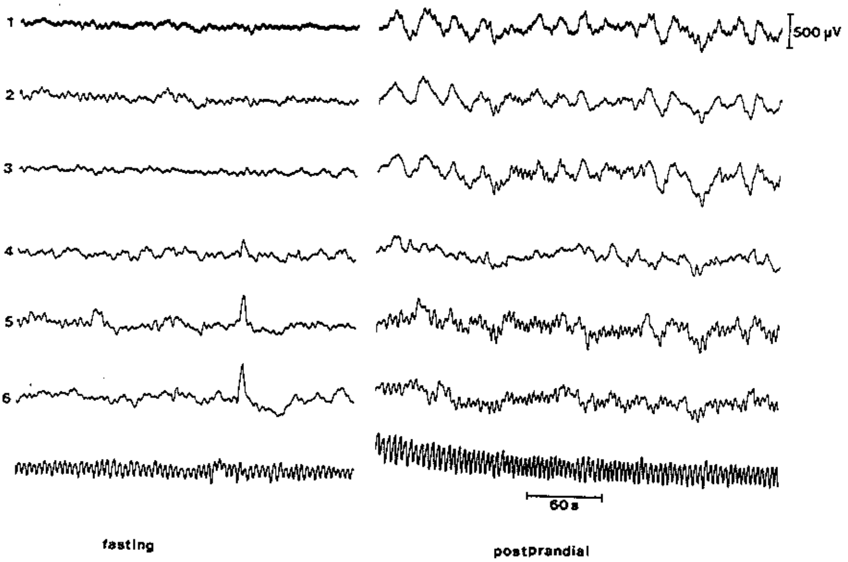

Fig.47 Typical unipolar abdominal signals (with respect to the right ankle) recorded in man. The lower trace shows the respiratory signal.

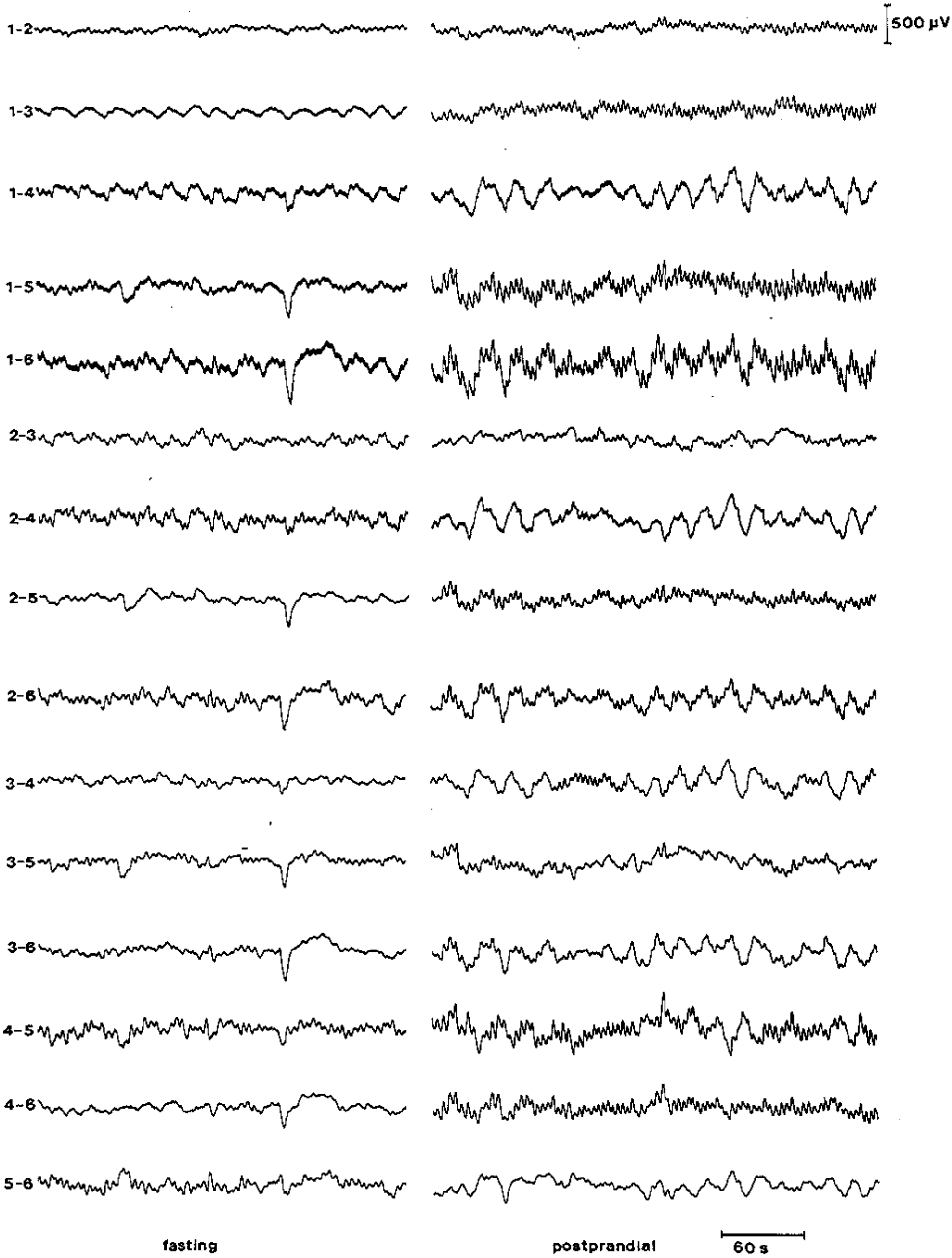

*Fig.48 Human bipolar electrogastrographic signals (obtained by means of subtraction of unipolar recorded signals).
Same signal fragments as in Fig.47.*

Fig.48 shows the bipolar signals obtained from the unipolar signals shown in Fig.47 by means of electronic subtraction. In this example it can be noted that, *in the fasting state,* the signals 1-3, 1-4, 2-3 and 2-4 exhibit gastric waves much more clearly than the corresponding unipolar signals. In 1-2 and 3-4 a gastric component can not be recognized visually. From these observations it can be concluded that, in this example, the unipolar signals 1 and 2 contain gastric waves that are (approximately) in phase; the same applies to the signals 3 and 4. It can further be concluded that the waves in 1 and 2 are (approximately) in counterphase with those in 3 and 4.

In the postprandial state the bipolar signals 1-4, 2-4, 1-6 and 2-6 are slightly 'better' than the unipolar signals 1, 2 and 3. The postprandial signals 1-2, 1-3, 2-3 and 4-6 hardly contain a visually recognizable gastric component. From these observations it can be concluded that the gastric waves in 1, 2 and 3 are (approximately) in phase, whereas these waves are (approximately) in counterphase with the waves in 4 and 6. It seems that two groups of signals with opposite polarity can be distinguished, both in the fasting and in the postprandial phase.
It further seems that the positions of the electrodes with respect to the stomach are different before and after the meal.
In order to investigate the validity of these findings, all unipolar and bipolar signals from our 17 volunteers were written out on chart. A score of 1, 2 or 3 was attached to each fasting and postprandial signal. A signal scored 1 when the gastric component was hardly recognizable at visual examination, 2 when the signal was of average quality and 3 when it was of more than average quality.
The following mean scores were found for the unipolar signals:

unipolar signal	mean score fasting	mean score postprandial
1	1.9	2.4
2	1.6	2.5
3	1.9	2.3
4	1.2	1.7
5	1.1	1.6
6	1.1	1.1

Both in the fasting and in the postprandial state the best unipolar signals were recorded from electrodes 1, 2 and 3.

The mean scores of the bipolar signals were:

bipolar signal	mean score fasting	mean score postprandial
1-2	1.5	1.5
1-3	2.3	1.9
1-4	2.0	2.8
1-5	2.0	2.0
1-6	2.2	2.2
2-3	2.2	2.0
2-4	1.9	2.8
2-5	1.5	1.4
2-6	1.7	2.1
3-4	2.0	2.4
3-5	1.5	1.4
3-6	1.9	2.0
4-5	1.5	2.2
4-6	1.0	1.7
5-6	1.1	1.6

In the fasting state the best bipolar signals were 1-3, 1-6 and 2-3, in the postprandial state 1-4, 2-4 and 3-4 scored highest.
Whereas the postprandial unipolar signal 4 scored low, the postprandial signals 1-4, 2-4 and 3-4 scored higher than the postprandial signals 1, 2 and 3. This finding is in accordance with the assumption that in the postprandial state, the gastric component in 4 is in counterphase with those in 1, 2 and 3.
In the fasting state, the gastric component in 3 probably is not in phase with the gastric component in 1 and 2, since 1-3 scored high and 1-2 did not.

5.6.3 Fourier analysis

Fig.49 shows the power spectra of the fasting and postprandial signal fragments shown in Fig.48.

In 80% of the stretches analyzed, a peak at about 0.05 Hz (3 cpm) was present; in the remaining 20% (mostly fasting state-stretches) such a peak could not be recognized. The latter percentage could be reduced by analyzing other bipolar signals, but this was not done in the present study.

In the power spectra studied, peaks at the duodenal frequency (11-12 cpm) were very rare, such in contrast with our findings in the dog.
The mean gastric frequency in the fasting state was 2.89 ± 0.17 cpm, the mean postprandial frequency was 3.01 ± 0.25 cpm.
For a somewhat more detailed study of the early postprandial frequency changes, all first postprandial 1024 s stretches were divided into two stretches of 512 s duration, and analyzed separately. Fig.50 shows the variations of the mean gastric frequency in our volunteers.

The frequency drop in the first two 512 s-stretches after the meal (1A and 1B) is not significant. The mean frequency of the second full postprandial stretch (from 1025 to 2048 s after the meal) differs significantly from the fasting frequency ($p = 0.02$).

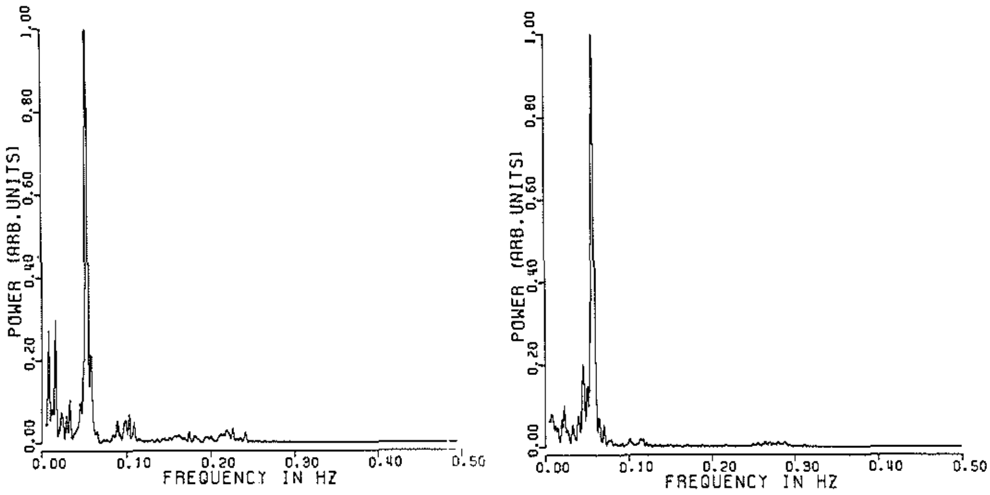

Fig.49 Power spectra of the 1-4 signal fragments shown in Fig.48.
Left spectrum : fasting state (gastric frequency 0.052 Hz or 3.11 cpm).
Right spectrum: postprandial state (gastric frequency 0.056 Hz or 3.34 cpm).

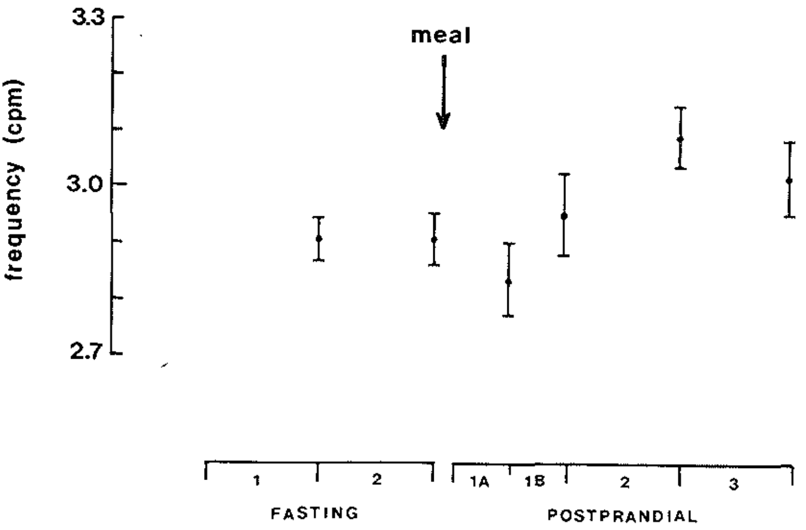

Fig.50 Mean gastric frequencies in 17 volunteers, fasting and after a test meal (+ s.e.m.). The bars are placed at the end of each 1024 s stretch. The first two postprandial bars concern stretches of 512 s duration (1a and 1b).

5.6.4 *Discussion*

The electrogastrographic signals recorded in man showed much resemblance to those recorded in the dog.
The electrogastrographic signals obtained from man and dog differed in the incidence of a duodenal component. Whereas a duodenal component was frequently seen in canine signals, its presence in man was very rare. The cause of this difference is not yet clear.
The mean gastric frequencies found in our human volunteers are in agreement with those found by Smallwood (1976). In 14 healthy volunteers Smallwood found (electrogastrographically) a mean fasting gastric frequency of 3.02 ± 0.21 cpm and a mean postprandial gastric frequency of 3.09 ± 0.27 cpm. Immediately following the meal a significant frequency drop was found. In another group of normal human beings a significantly different postprandial frequency (3.30 ± 0.25 cpm) was met (Smallwood, 1976). Smallwood hypothesized that this difference was due to the different age distributions of the two groups; the first group consisted of volunteers of 21 to 33 years of age, whereas the second group 'covered a much wider span of years'. The postprandial values found by us (in volunteers of 16 to 37 years of age) correspond to the postprandial values in Smallwood's first group and, therefore, are in accordance with Smallwood's hypothesis. Whether a correlation between gastric frequency and age really exists, remains an open question. Electrogastrography offers the means to answer it.
Regarding the electrode positions used in our studies in man, it can be concluded that positions 5 and 6 yielded little substantial information. These positions could be dropped in future studies.
The seemingly altered positions of the electrodes with respect to the stomach after the meal might be due to a postprandial shift of the distal stomach to the right, which is known to occur with gastric repletion (Hafferl, 1969).

5.7 *Conclusions*

- Recessed, pregelled, disposable Ag/AgCl electrocardiography-electrodes are suitable for electrogastrography.
- Bipolar abdominal leads yield the electrogastrographic signals with highest signal-to-noise ratio.
- Both ECA and ERA are reflected in the electrogastrogram.
- The sinusoidal configuration of the electrogastrogram as well as the ERA-related amplitude changes can be understood with the aid of a model in which depolarization and repolarization of gastric muscle are represented as dipoles.
- The postprandial cutaneous signal is characterized by a constant, high amplitude of the gastric component.
- During the phase motor quiescence of the IMC the amplitude of the gastric component is small.
- During the activity front periodic increases of the gastric waves in the cutaneous signal occur and low-frequency components of yet unknown origin are present.
- The IMC in the canine stomach, when present, can be detected with cutaneous electrodes.
- Tachygastrias can be recognized from the electrogastrogram.

- Canine electrogastrographical signals often contain a component with a frequency of about 19 cpm. This component originates from the duodenum.
- The electrogastrographic signals recorded in man show much resemblance to those recorded in the dog. In man the presence of a duodenal component in the cutaneous signal is rare, however.
- After a test meal, the frequency of the electrical activity of the human stomach falls and subsequently rises to above fasting levels. The amplitude of the gastric component in the cutaneous signal increases and probably the position of the gastric antrum with respect to the electrodes changes.

5.8 Appendix

Very recently, electrogastrographic indications of the presence of a tachygastria were found in a patient, one day after ileostomy. In the power spectrum of the electrogastrogram recorded from this patient (Fig.51) no significant gastric peak was observed, but an abnormal peak at 0.17 Hz (9.96 cpm) was found.

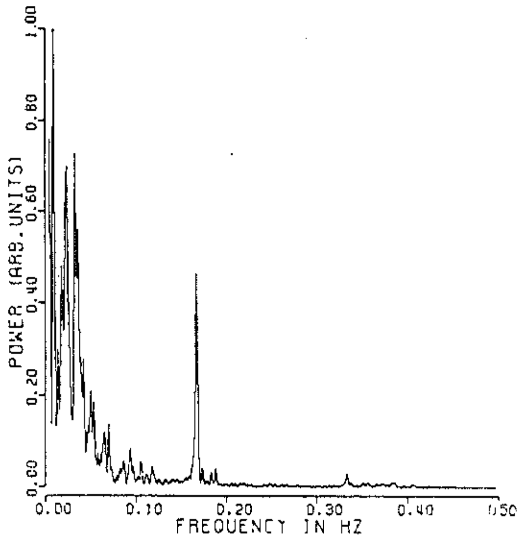

Fig.51 Powerspectrum of a 1024 s-stretch of human electrogastrographic signal (1-4), recorded from a patient one day after ileostomy. There is no significant gastric peak at 0.05 Hz, but a peak is seen at 0.17 Hz (9.96 cpm): the spectrum indicates the presence of a tachygastria.

6. FINAL CONCLUSIONS

The major objectives of our *gastroelectromyographic* and *electrogastrographic* studies were:

1. to answer the question 'What is measured?', and
2. to describe the characteristics of the recorded signals.

ad 1. We conclude that the initial potential of the *gastroelectromyographic* signal is the extracellular manifestation of membrane depolarization, the interpotential segment of the plateau phase, and the second potential of repolarization.
With the aid of a dipole model the *electrogastrographic* signal can be understood as resulting also from depolarization and repolarization of gastric smooth muscle cells.

ad 2. The configurations of the *gastroelectromyographic* signals are highly dependent upon the recording technique used.
The second potential, often neglected in the literature, is an essential, contraction-related component of the gastroelectromyographic signal. The rhythm of the Electrical Control Activity is not as regular as is often believed. Various ectopic and nonectopic dysrhythmias (arrhythmias) of the ECA can be observed in the stomach of the conscious dog.
In the dog, the *electrogastrographic* signals contain information about the frequency of the ECA, as well as about the postprandial and interdigestive myoelectrical patterns occurring in the stomach. Electrogastrographic explorations in man showed a good correspondence between the characteristics of canine and human electrogastrographic signals.

7. CLINICAL ASPECTS AND PERSPECTIVES

It seems unlikely that methods of recording the myoelectrical activity of the stomach will become important in the diagnosis of pathological changes in the gastric mucosa, such as peptic ulcer, carcinoma or gastritis. Recording of gastric myoelectrical activity might lead, however, to the discovery of hitherto unknown motor disorders of the stomach, or to the elucidation of mechanisms playing a role in the pathogenesis of 'known' gastric disorders.
A disorder of gastric myoelectrical activity which might become of clinical relevance is the tachygastria. As mentioned before, two patients with gastric retention-associated tachygastria have been described in recent literature (Telander et al., 1978; Sanders et al., 1979). Whereas all human tachygastrias hitherto reported have been diagnosed with invasive techniques, our studies made clear that noninvasive, electrogastrographic diagnosis of the tachygastria is possible.

In order to develop gastroelectromyography and especially electrogastrography to diagnostic tools, much research has still to be done.
Besides fundamental, basic studies, exploratory clinical studies are needed. In both types of research, close co-operation of medico-biological investigators and physicists must be considered indipensible.

SUMMARY

This thesis deals with the electrical activity of gastric smooth muscle. With the exception of the muscle in the most proximal gastric parts (cardia, fundus and upper portion of the corpus), gastric smooth muscle rhythmically generates 'action potentials'.

Chapter 1 is an introductory chapter in which a.o., the objectives of studies are formulated.

In Chapter 2 some relevant data concerning the anatomy of the stomach are summarized.

In Chapter 3 the literature on intracellular electrical activity of gastric muscle is surveyed.
The intracellularly recorded action potential exhibits a plateau of variable duration and amplitude. Spikes may occur superimposed upon the plateau. When the plateau is small or absent, the action potential is not followed by a phasic contraction. Phasic contractions can occur without spikes.

Chapter 4 deals with the method(s) of *gastroelectromyography*.
Firstly, the literature relevant for our studies is surveyed and the methods, materials and techniques used in our studies are described. Next, the signals that were recorded from the stomach of the conscious dog, using a monopolar technique, are described.
Every 12 seconds a so-called 'initial potential' arises from a pacemaker area in the orad corpus and subsequently propagates towards the pylorus. Only when this initial potential is followed by a 'second potential', a phasic contraction occurs. The configurations of these potentials are described. An attempt is made to elucidate the relation between the intracellularly recorded signal, known from literature, and the configurations of the extracellularly recorded initial and second potential and interpotential segment. Attention is paid to the relation between the amplitude of the phasic contraction and the configuration of the monopolar signal. Contractile force appears to increase with increasing amplitude of the second potential and with increasing duration of the interpotential segment. These findings can be understood on the basis of the results of intracellular studies surveyed in chapter 3 and the relation between intracellular and extracellular monopolar signals reasoned in chapter 4.
Next, the configurations of the signals recorded with our standard bipolar technique are described. An 'ERA score' is introduced. With the aid of this score, contractile activity can be assessed on the basis of the myoelectrical activity.
Subsequently, the *ectopic* arrhythmias (arrhythmias caused by initial potentials originating outside the normal pacemaker area) are described and discussed. Special attention is paid to the *tachygastrias*. These are arrhythmias in which an ectopic focus, mostly located in the antrum, generates initial potentials at an abnormally high frequency. During the presence of a tachygastria the stomach is mechanically inactive. Although tachygastrias of short duration are probably physiological, prolonged tachygastrias might be involved in the pathogenesis of gastric motor disorders. In our dogs, tachygastrias mainly occurred in the first week after operation.

In 'GASTRIC PACEMAKER RHYTHM IN CONSCIOUS DOG' the rhythm of the *nonectopic* initial potentials is described. The so-called activity front of the interdigestive myoelectric complex appears to be correlated with the periodic occurrence of considerably prolonged intervals between initial potentials. The motor quiescence phase of the interdigestive complex is correlated with small interval-to-interval variation, as is the early postprandial phase.

In Chapter 5 the method of *electrogastrography* (recording of gastric electrical activity from cutaneous electrodes) is studied.
Firstly, the literature on electrogastrography, dating from 1922 up to the present, is surveyed. This literature makes clear that gastric 'waves' can be recorded from the skin, but fails to make clear what exactly is measured in electrogastrography.
After paying attention to some technical aspects of recording electrogastrographical signals, an attempt is made to answer the question 'WHAT IS MEASURED IN ELECTROGASTROGRAPHY?'. On the basis of a study in the dog in which serosal and cutaneous signals are compared, a model is proposed. In the model the electrogastrographical signal is described as resulting from the presence of slowly propagating depolarization and repolarization dipoles. With the help of the model, the presence of a cutaneous signal during motor quiescence, the contraction-related amplitude increase and the 'sinusoidal' configuration of the electrogastrographical signal can be understood.
Next, the POSTPRANDIAL AND INTERDIGESTIVE GASTRIC ELECTRICAL ACTIVITY IN THE DOG RECORDED BY MEANS OF CUTANEOUS ELECTRODES, are described. It appears that the gastric interdigestive myoelectric complex, when present, can be recognized in the electrogastrographic signal. Furthermore, the electrogastrographic detection of tachygastria appears to be possible.
Finally, the results of some electrogastrographical explorations in man are presented. Most of the results obtained in man are in agreement with the results obtained in the dog. Best fasting and postprandial leads are selected by means of visual examination of the signals recorded on chart. Mean fasting and postprandial gastric frequencies are measured with the aid of spectral analysis.

SAMENVATTING

Dit proefschrift handelt over de elektrische aktiviteit van het gladde spierweefsel van de maag.
Met uitzondering van het spierweefsel in de meest proximale maagdelen (cardia, fundus en proximaal deel van het corpus) genereert het maagspierweefsel ritmische 'aktiepotentialen'.

Hoofdstuk 1 is een inleidend hoofdstuk waarin o.a. de vraagstellingen van onze onderzoekingen worden geformuleerd.

In Hoofdstuk 2 worden enige relevante gegevens betreffende de anatomie van de maag samengevat.

In Hoofdstuk 3 wordt een overzicht gegeven van de literatuur betreffende de intracellulaire elektrische aktiviteit van maagspierweefsel.
De intracellulair afgeleide aktiepotentiaal vertoont een plateau van variabele duur en amplitude, waarop spikes kunnen zijn gesuperponeerd. Wanneer het plateau klein is of ontbreekt, wordt de aktiepotentiaal niet gevolgd door een contractie. Voor de initiatie van een contractie zijn spikes niet vereist.

Hoofdstuk 4 handelt over de methode(n) van de *gastroelektromyografie*. Allereerst wordt de voor onze onderzoekingen relevante literatuur samengevat en worden de door ons gebruikte methoden, materialen en technieken beschreven.
Vervolgens worden de signalen die door ons met behulp van een monopolaire techniek van de maag van de wakkere hond werden afgeleid, beschreven. Vanuit een pacemakergebied in het corpus, aan de grote curvatuur, ontspringt iedere 12 seconden een zogenoemde 'eerste potentiaal', welke zich vervolgens in de richting van de pylorus verplaatst. Slechts wanneer deze eerste potentiaal gevolgd wordt door een 'tweede potentiaal', treedt een fasische contractie op.
De configuraties van deze beide potentialen worden beschreven.
Gepoogd wordt, licht te doen schijnen op de relatie tussen het intracellulair afgeleide signaal, zoals we dat kennen uit de literatuur, en de configuraties van de extracellulair afgeleide eerste en tweede potentiaal en het interpotentiale segment.
Aandacht wordt geschonken aan de relatie tussen de amplitude van de fasische contractie en de configuratie van het monopolaire signaal. De contractiekracht blijkt toe te nemen met toenemende amplitude van de tweede potentiaal en met toenemende duur van het interpotentiaal-segment. Deze bevindingen kunnen worden begrepen op grond van de resultaten van de intracellulaire onderzoekingen (samengevat in hoofdstuk 3) en de relatie tussen de intra- en extracelluairmonopolair signalen (beredeneerd in hoofdstuk 4). Daarna worden de configuraties van de met behulp van onze bipolaire standaardtechniek afgeleide signalen beschreven. We introduceren een 'ERA-score'. Met behulp van deze score kan de contractiekracht worden geschat op basis van de myoelektrische aktiviteit.
Daarna worden de *ectopische* aritmieën (verstoringen van de regelmaat door buiten het pacemakergebied ontspringende eerste potentialen) beschreven en besproken.
Hierbij wordt bijzondere aandacht geschonken aan de *tachygastrieën*. Dit zijn afwijkingen waarbij een ectopisch focus, meestal in het antrum gelegen, eerste potentialen met een abnormaal hoge frekwentie genereert.
Tijdens een tachygastrie is de maag motorisch inaktief. Alhoewel tachygastrieën

van korte duur vermoedelijk als physiologisch moeten worden beschouwd, zijn er aanwijzingen dat langdurige tachygastrieën pathogenetische betekenis zouden kunnen hebben. Bij onze honden werden tachygastrieën vooral gezien in de eerste week na implantatie van de elektroden.
In 'GASTRIC PACEMAKER RHYTHM IN CONSCIOUS DOG' wordt het ritme van *niet-ectopische* (uit het pacemakergebied ontspringende) eerste potentialen beschreven. Tijdens het zogeheten activiteitsfront van het interdigestieve myoelektrische complex blijken zich aanzienlijke, contractie-gerelateerde verlengingen van de intervallen tussen de eerste potentialen voor te doen. Tijdens de fase van motorische stilte van het interdigestieve complex is de interval-tot-interval variatie gering, evenals in de vroeg-postprandiale fase.

In Hoofdstuk 5 wordt de methode der *elektrogastrografie* (het van de huid afleiden van elektrische maagaktiviteit) bestudeerd.
Allereerst wordt een overzicht gegeven van de literatuur omtrent de elektrogastrografie, daterend van 1922 tot heden. Uit deze literatuur wordt duidelijk dat het mogelijk is maagaktiviteit van de huid af te leiden, maar het blijft onduidelijk wat men nu precies meet in de elektrogastrografie.
Nadat aandacht is besteed aan enige, de registratie van elektrogastrografische signalen betreffende, technische aspecten, wordt in "WHAT IS MEASURED IN ELECTROGASTROGRAPHY?' gepoogd door middel van vergelijking van serosa- en huidsignalen bij de hond een antwoord te vinden op de in de titel gestelde vraag. Onze uiteindelijke hypothese is, dat het huidsignaal teweeg wordt gebracht door de processen van depolarisatie en repolarisatie van het maagspierweefsel. Deze kunnen modelmatig worden voorgesteld als dipolen. Ons model is in overeenstemming met het feit dat ook tijdens motorische stilte een maagsignaal van de huid kan worden afgeleid, met het feit dat de amplitude van het huidsignaal toeneemt ten tijde van contracties en met de 'sinusoidale' configuratie van het elektrogastrografische signaal.
Vervolgens worden de kenmerken van het elektrogastrografische signaal tijdens de verschillende fasen van de digestieve en interdigestieve maagaktiviteit bij de wakkere hond beschreven in 'POSTPRANDIAL AND INTERDIGESTIVE GASTRIC ELECTRICAL ACTIVITY IN THE DOG RECORDED BY MEANS OF CUTANEOUS ELECTRODES'. Het blijkt dat het interdigestieve myoelektrische complex in de maag, indien aanwezig, elektrogastrografisch kan worden herkend. Tevens blijkt dat de aanwezigheid van tachygastrieën elektrogastrografisch kan worden vastgesteld.
Tenslotte worden de resultaten van enige elektrogastrografische verkenningen bij de mens beschreven. In grote lijnen zijn de bij de menselijke vrijwilligers verkregen resultaten in overeenstemming met die welke bij de hond werden verkregen. Door middel van visuele inspectie van de op papier geregistreerde signalen worden de beste nuchtere en postprandiale afleidingen geselecteerd. Met behulp van spectrale analyse worden de gemiddelde nuchtere en postprandiale maagfrekwenties bepaald.

REFERENCES

Aizawa, I., Hiwatshi, K., Takakashi, I., Itoh, Z. (1977)
"Control of motor activity in the lower esophageal sphincter by motilin".
In: "Gastrointestinal Motility in Health and Disease". Ed. H.L. Duthie.
MTP Press Lancaster; 101-111.

Allen, G.L., Poole, E.W., Code, C.F. (1964)
"Relationships between electrical activities of antrum and duodenum".
Am.J.Physiol., 207; 906-910.

Alvarez, W.C. (1922a)
"Action currents in stomach and intestine".
Am.J.Physiol. 58; 476-493.

Alvarez, W.C. (1922b)
"The electrogastrogram and what it shows".
J.A.M.A., 78; 1116-1119.

Alvarez, W.C. (1968)
"Early studies of the movements of the stomach and bowel".
In: "Handbook of Physiology", Section 6, Alimentary Canal, Vol. IV Motility.
Ed. C.F. Code.
Am.Physiol.Soc., Washington.

Bass, P., Code. C.F., Lambert E.H. (1961)
"Motor and electric activity of the duodenum".
Am.J.Physiol., 201; 287-291.

Bass, P., Wiley, J.N. (1972)
"Contractile force transducer for recording muscle activity in unanesthetized animals".
J.Appl.Physiol. 32; 567-570.

Bedi, B.S.,Kelly, K.A., Holley, K.E. (1972)
"Pathways of propagation of the canine gastric pacesetter potential".
Gastroenterology 63; 288-296.

Bessling, N.C., Van Maaren, D.Ch., Kingma, Y.J. (1976)
"An implantable biotelemetry transmitter for six differential signals".
Med.Biol.Eng. 14; 660-664.

Boev, K. (1972)
"On the correlation between the electric activity and the contraction of the smooth muscles".
Izv.Inst.Fiziol. (Sofia) 14; 163-169.

Boev, K., Golenhofen, K., Lukanow, J. (1976)
"Selective suppression of phasic and tonic activation mechanisms in stomach smooth muscle".
In : "Physiology of Smooth Muscle", ed. E.Bülbring and M.F.Shuba.
Raven Press, New York; 203-208.

Bortoff, A. (1961a)
"Slow potential variations of small intestine".
Am.J.Physiol. 201; 203-208.

Bortoff, A. (1961b)
"Electrical activity of intestine recorded with pressure electrode".
Am.J.Physiol. 201; 209-212.

Bortoff, A., Weg, N. (1965)
"Transmission of electrical activity through the gastroduodenal junction".
Am.J.Physiol. 208; 531-536.

Bortoff, A. (1967)
"Configuration of intestinal slow waves obtained by unipolar recording techniques".
Am.J.Physiol. 213; 157-162.

Bortoff, A. (1975a)
"Recording of extracellular electrical activity".
In: "Methods in Pharmacology", Volume 3, Smooth Muscle, ed. E.E.Daniel and D.M.Paton
Plenum Press, New York; 231-245.

Bortoff, A. (1975b)
"Electrical activity of gastrointestinal muscle".
In: "Functions of the stomach and intestine", ed. M.H.F.Friedman.
University Park Press, Baltimore.

Bortoff, A. (1976)
"Myogenic control of intestinal motility".
Physiol.Rev. 56; 418-434.

Bortolotti, M., Labo, G., Serantoni, C., Ciani, P. (1978)
"Effect of HSV on gastric motor activity of duodenal ulcer patients".
Digestion 17; 108-120.

Bozler, E. (1945)
"The action potentials of the stomach".
Am.J.Physiol. 144; 693-700.

Brown, B.H., Smallwood, R.H., Duthie, H.L., Stoddard, C.J. (1975)
"Intestinal smooth muscle electrical potentials recorded from surface electrodes".
Med.Biol.Eng. 13; 97-103.

Burnstock, G. (1970)
"Structure of smooth muscle and its innervation".
In: "Smooth Muscle", ed. E.Bülbring, A.F.Brading, A.W.Jones, T.Tomita.
Edward Arnold Publishers Ltd., London; 1-69.

Carlson, H.C., Code, C.F., Nelson, R.A. (1966)
"Motor action of the canine gastroduodenal junction: a cineradiographic, pressure and electric study".
Am.J.Dig.Dis. 11; 155-172.

Catchpole, B.N., Duthie, H.L. (1977)
"Postoperative gastrointestinal complexes".
In: "Gastrointestinal Motility in Health and Disease", ed. H.L.Duthie.
MTP Press, Lancaster; 33-42.

Civalero, L.A., Kanteliu, M. (1978)
"Simultaneous recording of gastric and duodenal electrical activity".
Sc.J.Gastr. 13; 459-463.

Coburn, R.F., Ohba, M., Tomita, T. (1975)
"Recording of intracellular electrical activity with the sucrose-gap method".
In: "Methods in Pharmacology", Volume 3, Smooth Muscle, ed. E.E.Daniel and D.M.Paton. Plenum Press, New York; 231-245.

Code, C.F., Szurszewski, J.H., Kelly K.A., Smith, I.B. (1968)
"A concept of control of gastrointestinal motility".
In: "Handbook of Physiology", Section 6, Alimentary Canal, Volume V.
Am.Physiol.Soc., Washington; 2881-2896.

Code, C.F., Carlson H.C. (1968)
"Motor activity of the stomach".
In: "Handbook of Physiology", Section 6, Alimentary Canal, Volume IV, chapter 93.

Code, C.F., Marlett, J.A. (1974)
"Canine tachygastria".
Mayo Clin. Proc. 49; 325-332.

Code, C.F., Marlett, J.A. (1975)
"The interdigestive myo-electric complex of the stomach and small bowel of dogs".
J.Physiol. (London), 246; 289-309.

Colombo, E., Mauri, A., Guzzo, M. (1978)
"Utilità della registrazione elettrica epicutanea per una diagnosi immediata di sede nelle occlusioni e sub-occlusioni intestinali".
Minerva Chirurgica 33; 1373-1376.

Combe, P., Thillier, J.L., Faucher, Cl., Martin, A., Regy, M. (1972)
"Apports de l'Electrogastroentérographie dans la pathologie digestive du nourisson".
Pediatrie 27; 483-495.

Daniel, E.E., Carlow, D.R., Wachter, B.T., Sutherland, W.H., Bogoch, A. (1959)
"Electrical activity of the small intestine".
Gastroenterology 37; 268-281.

Daniel, E.E., Chapman, K.M. (1963)
"Electrical activity of the gastrointestinal tract as an indicator of mechanical activity".
Am.J.Dig.Dis. 54; 54-102.

Daniel, E.E. (1965)
"The electrical and contractile activity of the pyloric region in dogs and the effects of drugs".
Gastroenterology 49; 403-418.

Daniel, E.E. (1966)
"Electrical and contractile response of the pyloric region to adrenergic and cholinergic drugs".
Can.J.Physiol.Pharmacol. 44; 951-979.

Daniel, E.E., Irwin, J. (1968)
"Electrical activity of gastric musculature".
In: "Handbook of Physiology", Section 6, Alimentary Canal, Volume IV.
Am.Physiol.Soc., Washington; 1969-1984.

Daniel, E.E., Daniel, V.P., Duchon, G., Garfield, R.E., Nichols, M., Malholtra, S.K., Oki, M. (1976)
"Is the nexus necessary for cell-to-cell coupling of smooth muscle?"
J.Membr.Biol. 28; 207-239.

Daniel, E.E., Sarna, S. (1978)
"Generation and conduction of activity in smooth muscle" (review).
Ann.R.Pharm. 18; 145-166.

Davis, R.C., Garafolo, L., Gault, F. (1957)
"An exploration of abdominal potentials".
J.Compar.Physiol.Psychol. 50; 529-532.

Dewey, M.M. (1965)
"The anatomical basis of propagation in smooth muscle".
Gastroenterology 49; 395-402.

Diamant, N.E., Hall, K., Mui, H., El-Sharkawy, T.Y. (1979)
"Vagal control of the feeding motor pattern in the lower esophageal sphincter, stomach and upper small intestine of dog".
Proc. 7th Int.Symp. on Gastrointestinal Motility (Iowa City)
Raven Press, New York (in press).

Drieux, C. Garnier, D., Marin, A., Moline, J. (1978)
"Correlation between variations of electrical field at the body surface and contractions of the stomach in the guinea-pig".
J.Physiol. (Paris) 74; 703-707.

Duthie, H.L., Kwong, N.K., Brown, B.H., Whittaker, G.E. (1971)
"Pacesetter potential of the human gastroduodenal junction".
Gut 12; 250-256.

Edwards, D.A.W., Rowlands, E.N. (1968)
"Physiology of the gastroduodenal junction".
In: "Handbook of Physiology", Section 6, Alimentary Canal, Volume IV, Motility.
Am.Physiol.Soc., Washington, 1985-2000.

Eeckhout, C., De Wever, I., Peeters, T., Hellemans, J., Vantrappen, G. (1978)
"Role of gastrin and insulin in postprandial disruption of migrating complex in dogs."
Am.J.Physiol. 235; E666-669.

El-Sharkawy, T.Y., Morgan, K.G., Szurszewski, J.H. (1978)
"Intracellular electrical activity of canine and human gastric smooth muscle".
J.Physiol. (London) 279; 291-307.

El-Sharkawy, T.Y., Szurszewski, J.H. (1978)
"Modulation of canine antral circular smooth muscle by acetylcholine and pentagastrin".
J.Physiol. (London) 279; 309-320.

Fleckenstein, P. (1978)
"Migrating electrical spike activity in fasting human small-intestine".
Am.J.Dig.Dis. 23; 769-775.

Geddes, L.A., Baker, L.E. (1967)
"The specific resistance of biological material - a compendium of data for the biomedical engineer and physiologist".
Med.Biol.Eng. 5; 271-293.

Geddes, L.A., Baker, L.E. (1968)
"Principles of applied biomedical instrumentation".
John Wiley & Sons Inc., New York.

Geddes, L.A. (1972)
"Electrodes and the measurement of bioelectric events".
Wiley Interscience, New York.

Golenhofen, K., Von Loh, D., Milenov, K. (1970)
"Elektrophysiologische Forschungen zur Spontanaktivität in isolierter Muskelpräparate aus verschiedene Abschnitten des Meerschweinchen-Magens".
Pflügers Arch. 315; 336-356.

Grivel, M.L., Ruckebusch, Y. (1972)
"The propagation of segmental contractions along the small intestine".
J.Physiol. (London) 227; 611-625.

Hafferl, A. (1969)
"Lehrbuch der topographischen Anatomie", 3. Auflage.
Springer Verlag, Berlin; p.464.

Henderson, R.M. (1975)
"Cell-to-cell contacts".
In: Methods in Pharmacology", Vol. 3, Smooth Muscle. Ed. E.E.Daniel and D.M.Paton
Plenum Press, New York.

Hiesinger, E., Hoernicke, H., Ehrlein, H-J. (1977)
"Computer analysis of electrical and mechanical activity of stomach, duodenum and cecum over long periods".
In: "Gastrointestinal Motility in Health and Disease", ed. H.L.Duthie.
MTP Press, Lancaster; 275-284.

Hinder, R.A., Kelly, K.A. (1977)
"Human gastric pacesetter potential. Site of origin, spread and response to gastric transection and proximal gastric vagotomy".
Am.J.Surg. 133; 29-33.

Hubel, K.A., Follick, M.A. (1976)
"A small strain gage for measuring intestinal motility in rats".
Am.J.Dig.Dis. 21; 1075-1078.

Ingram, P.W., Richards, D.L. (1953)
"Observations of potential difference of the human stomach by a new electrode and measuring system."
Gastroenterology 25; 273-289.

Itabisashi, T. (1964a)
"Electrophysiological studies on the movement of the ruminant stomach".
Part I. Nat.Inst.Anim.Health Quart. 4; 92-103.

Itabisashi, T. (1964b)
"Electrophysiological studies on the movement of the ruminant stomach".
Part III. Nat.Inst.Anim.Health Quart. 4; 115-124.

Itabisashi, T., Matsumoto, H. (1964)
"Electrophysiological studies on the movement of the ruminant stomach."
Part II. Nat.Inst.Anim.Health Quart. 4; 104-114.

Itabisashi, T. (1965)
"Electrophysiological studies on the movement of the ruminant stomach. Supplementary examination."
Nat.Inst.Anim.Health Quart. 5; 97-103.

Itabisashi, T., Matsumoto, H. (1966)
"Eelctrophysiological studies on the movement of the ruminant stomach."
Part IV. Nat.Inst.Anim.Health Quart. 6; 43-55.

Itoh, Z., Honda, R., Hiwatashi, K., Takeuchi, S., Aizawa, I., Takayanagi, R., Couch, E.F. (1976)
"Motilin induced mechanical activity in the canine alimentary tract."
Scand.J.Gastroent. 11 S39; 93-110.

Itoh, Z., Aizawa, I., Takeuchi, S., Takayanagi, R. (1977)
"Diurnal changes in gastric motor activity in conscious dogs".
Am.J.Dig.Dis. 22; 117-124.

Itoh, Z., Honda, R., Aizawa, I., Takeuchi, S., Hiwatashi, K., Couch, E.F.(1978a)
"Interdigestive motor activity of the lower esophageal sphincter in the conscious dog."
Am.J.Dig.Dis. 23; 239-247.

Itoh, Z., Takeuchi, S., Aizawa, I., Takayanagi, R. (1978b)
"Characteristic motor activity of gastrointestinal tract in fasted conscious dogs measured by implanted force transducers".
Am.J.Dig.Dis. 23; 229-238.

Itoh, Z., Honda, R., Takeuchi, S., Aizawa, I. (1979)
"Regular and irregular control of interdigestive contractions by motilin and intraduodenal pH."
Proc. 7th Int. Symposium on Gastrointestinal Motility (Iowa City)
Raven Press, New York (in press).

Jacoby, H.I., Bass, P., Bennett, D.R. (1963)
"In vivo extraluminal force transducer for gastrointestinal muscle".
J.Appl.Physiol. 18; 658-665.

Kelly, K.A., Code, C.F. (1969)
"Effect of transthoracic vagotomy on canine gastric electrical activity".
Gastroenterology 57; 51-58.

Kelly, K.A., Code, C.F., Elveback, L.R. (1969)
"Patterns of canine gastric electrical activity".
Am.J.Physiol. 217; 461-470.

Kelly, K.A., Code, C.F. (1971)
"Canine gastric pacemaker".
Am.J.Physiol. 220; 112-118.

Kelly, K.A., La Force, R.C. (1972)
"Pacing the canine stomach with electrical stimulation".
Am.J.Physiol. 222; 588-594.

Kingma, Y.J., Van der Schee, E.J., Grashuis, J.L. (1975)
"Implantable transducer for sensing contractions of the stomach wall and intestine".
Proc.Int.Conf.on Biomedical Transducers (Biocapt), Paris; Tome I, 69-74.

Kingma, Y.J. (1977)
"Measurements on glassy-carbon electrodes in saline".
Med.Biol.Eng.Comput. 15; 327-332.

Kosterlitz, H.W. (1968)
"Intrinsic and extrinsic nervous control of motility of the stomach and the intestines."
In: "Handbook of Physiology", Section 6, Alimentary Canal, Volume IV, Motility.
Am.Physiol.Soc., Washington; 2147-2171.

Kwong, N.K., Brown, B.H., Whittaker, G.E., Duthie, H.L. (1970)
"Electrical activity of gastric antrum in man".
Br.J.Surg. 57; 913-916.

Linkens, D.A. (1977)
"Methods of analysing rhythmic electrical potentials in the gastrointestinal tract."
In: Gastrointestinal Motility in Health and Disease", ed. H.L.Duthie.
MTP Press Lancaster; 235-249.

Lux, G., Lederer, P., Femppel, J., Rösch, W., Domschke, W. (1979)
"Spontaneous and 13-NLE-Motilin induced interdigestive motor activity of esophagus, stomach and small intestine in man."
Proc. 7th Int.Symp.on Gastrointestinal Motility (Iowa City).
Raven Press, New York (in press).

Marik, F., Code, C.F. (1975)
"Control of the interdigestive myoelectric activity in dogs by the vagus nerves and pentagastrin."
Gastroenterology 69; 387-395.

Martin, A., Thouvenot, J., Touron, P. (1967)
"Variations périodiques des potentiels cutanés abdominaux en relation avec l'activité digestive".
C.R.Soc.Biol. 161; 2595-2600.

Martin, A., Thouvenot, J., Masson, J-M., Touron, P. (1970)
"Interet et place de l'électrosplanchnographie en pathologie psychosomatique digestive".
Ann.Méd.-Psychol. 128; 31-41.

Martin, A., Moline, J., Murat, J. (1971)
"Apport de l'électrosplanchnographie (ESG) au diagnostic préoperatoire d' une ulcération gastrique".
Presse Médicale 79; 1277-1278.

Martin, A., Thillier, J.L. (1971a)
"L'électrogastroentérographie (EGEG)."
C.R.Soc.Biol. 165; 1727-1733.

Martin, A., Thillier, J.L. (1971b)
"Un viscère digestif en activité, possède-t-il un axe électrique?"
C.R.Soc.Biol. 165; 1704-1711.

Martin, A., Thillier, J.L. (1972)
"La vectogastrogramme. Moyen de compréhension et de validation de l'électrogastroentérographie."
Nouv.Presse Med. 1; 453-456.

Martin, A., Thillier, J.L., Moline, J. (1972)
"Effets de la section du vague sur la motricité gastrique chez l'Homme. Etude électrogastroentérographique."
J.Physiol. (Paris) 65; 145A.

McCoy, E.J., Bass, P. (1963)
"Chronic electrical activity of gastroduodenal area: effects of food and certain catecholamines."
Am.J.Physiol. 205; 439-445.

Mendel, C., Pousse, A., Lambert, A., Grenier, J.F. (1979)
"Recording of canine intestinal chronic longitudinal movements."
Proc. 7th Int. Symposium on Gastrointestinal Motility (Iowa City).
Raven Press, New York (in press).

Milenov, K. (1968)
"Electrical and motor activities of the stomach after partial resections of the small and big curvature".
Izvest.Instit.Fiziol. (Sofiya) 11; 79-96.

Milenov, K., Boev, K. (1972)
"Bioelectric activity of the stomach in guinea pigs."
Izvest.Instit.Fiziol. (Sofiya) 14; 151-161.

Morgan, K.G., Szurszewski, J.H. (1978)
"Simultaneous measurement of mechanical and intracellular electrical activity of canine corporal smooth muscle-effects of acetylcholine and potassium."
(Meeting abstract) Fed.Proc. 37; 227.

Morgan, K.G., Go, V.L.W., Szurszewski, J.H. (1979)
"Motilin increases the influence of excitatory myenteric plexus neurons on gastric smooth muscle in vitro."
Proc. 7th Int. Symposium on Gastrointestinal Motility (Iowa City).
Raven Press, New York (in press).

Mroz, C.T., Kelly, K.A. (1977)
"Role of extrinsic antral nerves in regulation of gastric emptying".
Surg.Gyn.Obst. 145; 369-377.

Nechiporuk, V.M., Kasakov, V.N., Nakhlis, Z.Sh. (1973)
"Electrogastrographic investigations in the clinical picture of inflammatory diseases of the pancreas." (In Russian).
Klin.Med. 2; 87-89.

Nelsen, T.S., Eigenbrodt, E.H., Keoshian, L.A., Bunker, C., Johnson, L. (1967)
"Alterations in muscular and electrical activity of the stomach following vagotomy".
Arch.Surg. 94; 821-835.

Nelsen, T.S. (1967)
"Use of phaselock techniques for retrieval of the electrogastrogram from cutaneous and swallowed electrodes".
Dig. 7th Int.Conf. on Medical and Biological Engineering; 23.3.

Nelsen, T.S., Kohatsu, S. (1968)
"Clinical electrogastrography and its relation to gastric surgery".
Am.J.Surg. 116; 215-222.

Ohba, M., Sakomoto, Y., Tomita, T. (1975)
"The slow wave in the circular muscle of the guinea-pig stomach".
J.Physiol. (London) 253; 505-516.

Ohba, M., Sakomoto, Y., Tomita, T. (1977)
"Effects of sodium, potassium and calcium-ions on slow wave in circular muscle of guinea-pig stomach."
J.Physiol. (London) 267; 167-180.

O'Leary, J.F., Hennessy, T.P. (1977)
"Myoelectrical activity of canine stomach and duodenum after gastric resection".
J.Surg.Res. 23; 161-165.

Ormsbee III H.S., Mir, S.S. (1977)
"The role of the cholinergic nervous system in the gastrointestinal response to motilin in vivo."
In: "Gastrointestinal Motility in Health and Disease", ed. H.L.Duthie.
MTP Press, Lancaster; 113-123.

Papasova, M.P., Nagai, T., Prosser, C.L. (1968)
"Two component slow waves in smooth muscle of cat stomach".
Am.J.Physiol. 214; 695-702.

Papasova, M., Boev, K. (1976)
"The slow potential and its relationship to the gastric smooth muscle contraction."
In: "Physiology of Smooth Muscle", ed. E.Bülbring and M.F.Shuba.
Raven Press, New York; 209-216.

Papasova, M., Altaparmacov, I., Mavrov, N. (1976)
"Combined probe for recording the electric activity of the gastrointestinal tract in man."
Doklady Bolbarskoi Akademii Nauk 29; 1071-1074.

Peeters, T.L., Vantrappen, G., Janssens, J. (1979)
"Fluctuations of motilin and gastrin levels in relation to the interdigestive motility complex in man."
Proc. 7th Int. Symposium on Gastrointestinal Motility (Iowa City).
Raven Press, New York (in press).

Plonsey, R. (1969)
"Bioelectric phenomena".
McGraw-Hill Inc., New York.

Reverdin, N. Hutton, M., Ling, A., Thompson, H.H., Wingate, D.L., Christofides, N., Adrian, T.E., Bloom, S.R. (1979)
"Vagotomy and the motor response to feeding."
Proc. 7th Int. Symposium on Gastrointestinal Motility (Iowa City).
Raven Press, New York (in press).

Richter, C.P. (1924)
"Action currents from the stomach."
Am.J.Physiol. 67; 612-633.

Rosenquist, C.J., Carrigg, J.W., Regal, A-M.Y., Kohatsu, S. (1977)
"Electrical, contractile and radiographic studies of stomach after proximal gastric vagotomy."
Am.J.Surg. 134; 338-342.

Ruckebusch, Y., Bueno, L. (1976)
"The effect of feeding on the motility of the stomach and small intestine in the pig."
Br.J.Nutr. 35; 397-405.

Ruckebusch, Y., Bueno, L. (1977)
"Migrating myoelectrical complex of small intestine-intrinsic activity mediated by vagus."
Gastroenterology 73; 1309-1314.

Russell, R.W.,Stern, R.M. (1967)
"Gastric Motility: the electrogastrogram."
In: "A manual of Psychophysiological Methods". Ed. P.H.Venables and I.Martin.
North-Holland Publ.Cy., Amsterdam.

Sanders, K., Menguy,R., Chey, W., You, C., Lee, K., Morgan, K., Kreulen, D., Schmalz, P., Muir, T., Szurszewski, J. (1979)
"One explanation for human antral tachygastria." (Abstract)
Gastroenterology 76; 1234.

Sanders, K.M., Szurszewski, J.H. (1979)
"Endogenous prostaglandin and control of gastric motility."
Proc. 7th Int. Symposium on Gastrointestinal Motility (Iowa City).
Raven Press, New York (in press).

Sarna,S.K., Daniel, E.E., Kingma, Y.J. (1972a)
"Simulation of the electric control activity of the stomach by an array of relaxation oscillators."
Am.J.Dig.Dis. 17; 299-310.

Sarna, S.K., Daniel, E.E., Kingma, Y.J. (1972b)
"Premature control potentials in the dog stomach and in the gastric computer model."
Am.J.Physiol. 222; 1518-1523.

Sarna, S., Daniel, E., Kingma, Y. (1972c)
"Effects of partial cuts on gastric electrical control activity and its computer model".
Am.J.Physiol. 223; 332-340.

Sarna, S.K., Daniel, E.E. (1973)
"Electrical stimulation of gastric electrical control activity."
Am.J.Physiol. 225; 125-131.

Sarna, S.K., Daniel, E.E. (1974)
"Threshold curves and refractoriness properties of gastric relaxation oscillators."
Am.J.Physiol. 226; 749-755.

Sarna, S.K. (1975)
"Gastrointestinal electrical activity: terminology."
Gastroenterology 68; 1631-1635.

Schulz, J., Reitzig, P., Schulze, E., Bärsch, J., Etzold, H., Lisewski, G.(1973)
"Ueber die Aussagemöglichkeiten der Elektrogastroenterographie."
Dt.Gesundh.-Wesen 28; 2485-2488.

Schulz, J., Kramer, H.J., Lisewski, G., Schulze, E., Reitzig, P. (1976)
"Pharmakologische Beeinflussung der Motilität des Magen-Darm-Traktes."
Dt.Gesundh.-Wesen 31; 2150-2152.

Schuurkes, J.A.J., Van der Schee, E.J., Grashuis, J.L. (1977)
"Calibration of strain-gauge force transducers and quantification of gastric motility."
In: "Gastrointestinal Motility in Health and Disease". Ed. H.L.Duthie.
MTP Press, Lancaster; 647-654.

Smallwood, R.H., Brown, B.H., Duthie, H.L. (1975)
"An approach to the objective analysis of intestinal smooth muscle potentials recorded from surface electrodes."
Proc. 5th Int. Symposium on Gastrointestinal Motility, Leuven, Belgium.

Smallwood, R.H. (1976)
"Gastrointestinal electrical activity from surface electrodes."
Thesis, Sheffield, England.

Smallwood, R.H. (1978a)
"Analysis of gastric electrical signals from surface electrodes using phase-lock techniques." Part 1 - System design.
Med.Biol.Eng.Comp. 16; 507-512.

Smallwood, R.H. (1978b)
"Analysis of gastric electrical signals from surface electrodes using phase-lock techniques." Part 2 - System performance with gastric signals.
Med.Biol.Eng.Comp. 16; 513-518.

Smout, A.J.P.M., Van der Schee, E.J., Grashuis, J.L. (1979a)
"Gastric pacemaker rhythm in conscious dog."
Am.J.Physiol. 237; E279-E283.

Smout, A.J.P.M., Van der Schee, E.J., Grashuis, J.L. (1979b)
"Postprandial and interdigestive gastric electrical activity in the dog recorded by means of cutaneous electrodes."
Proc. 7th Int. Symposium on Gastrointestinal Motility (Iowa City).
Raven Press, New York (in press).

Smout, A.J.P.M., Van der Schee, E.J., Grashuis, J.L. (1980)
"What is measured in Electrogastrography?"
Dig.Dis.Sci. (in press).

Sobakin, M.A., Smirnov, I.P., Mishin, L.N. (1962)
"Electrogastrography."
IRE Trans.Bio.Med.Electron. 9; 129-132.

Sobakin, M.A., Privalov, I.A. (1976)
"Multichannel recording of human gastric electrical activity from body surface."
Bull.Exp.Biol.Med. 81; 636-638.

Stevens, J.K., Worrall, N. (1974)
"External recording of gastric activity: the electrogastrogram."
Physiol.Psychol. 2; 175-180.

Stoddard, C.J., Smallwood, R.H., Brown, B.H., Duthie, H.L. (1975)
"The immediate and delayed effects of different types of vagotomy on human gastric myoelectrical activity."
Gut, 16; 165-170.

Stoddard, C.J., Smallwood, R.H., Duthie, H.L. (1977)
"Migrating myoelectrical complexes in man."
In: "Gastrointestinal Motility in Health and Disease." Ed. H.L.Duthie.
MTP Press, Lancaster; 9-17.

Swanson, D.K., Webster, J.G. (1974)
"A model for skin-electrode impedance."
In: "Biomedical electrode technology-theory and practice." Ed. H.A.Miller and D.C.Harrison.
Academic Press Inc., New York.

Szurszewski, J.H. (1969)
"A migrating electrical complex of the canine small intestine."
Am.J.Physiol. 217; 1757-1763.

Szurszewski, J.H. (1975)
"Mechanism of action of pentagastrin and acetylcholine on the longitudinal muscle of the canine antrum."
J.Physiol. (London) 252; 335-361.

Taylor, I., Duthie, H.L., Smallwood, R., Linkens, D. (1975)
"Large bowel myoelectric activity in man."
Gut 16; 808-814.

Telander, R.L., Morgan, K.G., Kreulen, D.L., Schmalz, P.F., Kelly, K.A. Szurszewski, J.H. (1978)
"Human gastric atony with tachygastria and gastric retention."
Gastroenterology 75; 497-501.

Thomas, P.A., Kelly, K.A., Go, V.L.W. (1979)
"Does motilin regulate canine interdigestive gastric motility?"
Dig.Dis.Sci. 24; 577-582.

Thouvenot, J., Tonkovic, S., Penaud, J. (1973)
"Electrosplanchnography: method for the electrophysiological exploration of the digestive tract."
Acta Med. Iugoslav. 27; 227-247.

Tiemann, F., Reichertz, P. (1959a)
"Experimentelle Grundlagen des Elektrointestinogramms."
Med.Exptl. 1; 17-26.

Tiemann, F., Reichertz, P. (1959b)
"Ueber das intestinale Elektrogramm (EIG) und seine Bedeutung für die Klinik."
Med.Klin. 54; 654-656.

Tonkovic, S., Penaud, J., Thouvenot, J., Mountafian, J.P. (1975)
"Une application de l'analyse spectrale dans le traitement des signaux électrosplanchnografiques".
Med.Biol.Eng. 13; 266-271.

Tonkovic, S., Thouvenot, J., Penaud, J. (1976)
"Electrosplanchnographical exploration of the digestive tract diseases."
Dig. of 11th Int.Conf. on Med. and Biol. Eng., Ottawa.

Torgersen, J. (1942)
"The muscular build and movements of the stomach and duodenal bulb."
Acta Radiol. Suppl. 45; 1-191.

Vantrappen, G., Janssens, J., Hellemans, J., Christofides, N., Bloom, S. (1977a)
"Studies on the interdigestive (migrating) motor complex in man."
In: Gastrointestinal Motility in Health and Disease." Ed. H.L.Duthie.
MTP Press, Lancaster; 3-8.

Vantrappen, G., Janssens, J., Hellemans, J., Ghoos, Y. (1977b)
"Interdigestive motor complex of normal subjects and patients with bacterial overgrowth of small intestine."
J.Clin.Invest. 59; 1158-1166.

Walker, B.B., Sandman, C.A. (1977)
"Physiological response patterns in ulcer patients. Phasic and tonic components of the electrogastrogram".
Psychophysiology 14; 393-400.

Walker, B.B., Lawton, C.A., Sandman, C.A. (1978)
"Voluntary control of electro-gastric activity."
Psychosoc.Med. 40; 610-619.

Weber, J., Kohatsu, S. (1970)
"Pacemaker localization and electrical conduction patterns in the canine stomach".
Gastroenterology 59; 717-726.

Weisbrodt, N.W., Copeland, E.M., Kearly, R.W., More, E.P., Johnson, L.R. (1974)
"Effects of pentagastrin on electrical activity of small intestine of the dog."
Am.J.Physiol. 227; 425-429.

Weisbrodt, N.W., Copeland, E.M., More, E.P. (1975)
"Effect of vagotomy on electrical activity of small intestine of the dog."
Am.J.Physiol. 228; 650-654.

De Wever, I., Eeckhout, C., Vantrappen, G., Hellemans, J. (1978)
"Disruptive effect of test meals on interdigestive motor complex in dogs."
Am.J.Physiol. 235; E661-665.

Wilbur, B.G., Kelly, K.A. (1973)
"Effect of proximal gastric, complete gastric and truncal vagotomy on canine electric activity, motility and emptying."
Ann.Surg. 178; 295-303.

Wingate, D.L., Ruppin, H., Green, W.E.R., Thompson, H.H., Domschke, W., Wünsch, E., Demling, L., Ritchie, H.D. (1976)
"Motilin induced electrical activity in the canine gastrointestinal tract."
Scand.J.Gastr. 11 (S39); 111-118.

Wingate, D.L., Thompson, H.H., Pearce, E.A., Dand, A. (1977)
"The effects of exogenous cholecystokinin and pentagastrin on myoelectrical activity in the small intestine of the conscious fasted dog."
In: "gastrointestinal Motility in Health and Disease." Ed. H.L.Duthie.
MTP Press, Lancaster; 47-60.

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De schrijver van dit proefschrift werd op 19 juni 1950 te Amsterdam geboren. Na het gymnasium-ß diploma te hebben behaald, begon hij in 1968 met de studie der geneeskunde aan de Universiteit van Amsterdam. In de jaren 1971/1972 en 1972/1973 was hij kandidaat-assistent bij het Fysiologisch Laboratorium van bovengenoemde universiteit (hoofd: prof.dr. J.Th.F. Boeles). Het artsexamen werd in 1975 afgelegd.
Van 1 juli 1975 tot 1 juli 1976 was de schrijver werkzaam als arts-assistent op de afdeling Inwendige Geneeskunde van het Diaconessenhuis te Voorburg (hoofd: dr. P.C. Brinkerink).
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