

Intestinal tachyarrhythmias during small bowel ischemia

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Seidel, Scott A., Sanjay S. Hegde, L. Alan Bradshaw, J. K. Ladipo, and William O. Richards. Intestinal tachyarrhythmias during small bowel ischemia. *Am. J. Physiol.* 277 (*Gastrointest. Liver Physiol.* 40): G993–G999, 1999.—The electrical control activity (ECA) of the bowel is the omnipresent slow electrical wave of the intestinal tract. Characterization of small bowel electrical activity during ischemia may be used as a measure of intestinal viability. With the use of an animal model of mesenteric ischemia, serosal electrodes and a digital recording apparatus utilizing autoregressive spectral analysis were used to monitor the ECA of 20 New Zealand White rabbits during various lengths of ischemia. ECA frequency fell from 18.2 ± 0.5 cycles per minute (cpm) at baseline to 12.2 ± 0.9 cpm ($P < 0.05$) after 30 min of ischemia and was undetectable by 90 min of ischemia in all animals. Tachyarrhythmias of the ECA were recorded in 55% of the animals as early as 25 min after ischemia was induced and lasted from 1 to 48 min. Frequencies ranged from 25 to 50 cpm. These tachyarrhythmias were seen only during ischemia, suggesting that they are pathognomonic for intestinal ischemia. The use of the detection of ECA changes during intestinal ischemia may allow earlier diagnosis of mesenteric

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THE SEVERE MORBIDITY and mortality of mesenteric ischemia is largely due to delayed diagnosis and, consequently, the advanced stage of disease at laparotomy (21). The detection of mesenteric ischemia is one of the most difficult and challenging diagnoses for the clinician to make, often requiring invasive diagnostic procedures such as angiography (with its own inherent risks) or laparotomy. There are no noninvasive lab tests with sufficient specificity or sensitivity that have proven useful in the diagnosis of mesenteric ischemia (2, 5, 13, 21). To improve the prognosis in these patients, a more effective means of detecting mesenteric ischemia must be found. Ideally, such a test would be sensitive, specific, noninvasive, quick, repeatable, and easily performed in critically ill patients.

Our lab has been involved in characterizing the effects of acute mesenteric ischemia on the electrical control activity (ECA) of the small intestine to enable the use of ECA (also known as the basic electrical rhythm or BER) to predict bowel viability during

ischemia. The frequency and amplitude of small bowel ECA have been previously shown to fall with arterial ischemia (7, 16, 18, 20). These changes have also been shown to occur before the onset of pathological changes (11). Characterization of the electrical properties of the ischemic ECA signal are important in identification of the signature of ischemia. The studies reported here were designed to prolong ischemia long enough for the ECA frequency to fall to undetectable levels to enable the full characterization of the relationship between mesenteric ischemia and ECA. During serosal electrode recordings of ECA, we recorded multiple intestinal tachyarrhythmias of various frequencies during ischemia. This is the first demonstration of intestinal tachyarrhythmias. Because these arrhythmias have been recorded only during acute ischemia, they appear to be pathognomonic for small bowel ischemia.

MATERIALS AND METHODS

Twenty male New Zealand White rabbits weighing ~4 kg each were divided into four study groups that were subjected to different lengths of intestinal ischemia (90–210 min). General anesthesia was induced with acepromazine (0.5 mg/kg), xylazine (3 mg/kg), and ketamine (40 mg/kg) intramuscularly, and an intravenous catheter was placed for saline and intravenous ketamine to maintain anesthesia. Temperature was kept constant ($\pm 5^\circ\text{F}$) with a heating blanket and monitored with a rectal thermometer. A Silastic four-channel electrode platform connected by shielded wires to a Beckman amplifier (model R612) was sutured to a segment of proximal jejunum after a laparotomy was performed. The bowel was returned to the abdomen in a nonconducting latex glove (to prevent the recording of ECA from adjacent loops of bowel). Data (ECA signals) were sampled at a frequency of 20 Hz, with bandpass filters set from 0.016 Hz to 0.3 Hz. The amplifier was equipped with a 16-bit analog-to-digital converter (model MP100, Biopac Systems) into an Apple Powerbook (Apple Computer) utilizing Acqknowledge 3.1.2 software (Biopac Systems). All experiments were performed in an electrically shielded room to minimize background electrical interference. Baseline ECA recordings were performed for 15–30 min, after which we induced ischemia by transecting the segment of bowel proximally and distally to prevent intramural blood flow and by occluding the segmental artery and vein using a vascular occluder. Complete ischemia was confirmed with a Doppler flow probe (model ES-1000SPM, Koven Technology). The bowel was then placed back into the abdomen in the latex glove. Varying lengths of complete ischemia were maintained (90, 120, 150, and 210 min for groups 1, 2, 3, and 4, respectively) while continuous recordings of ECA were made. At the end of the study each animal was euthanized.

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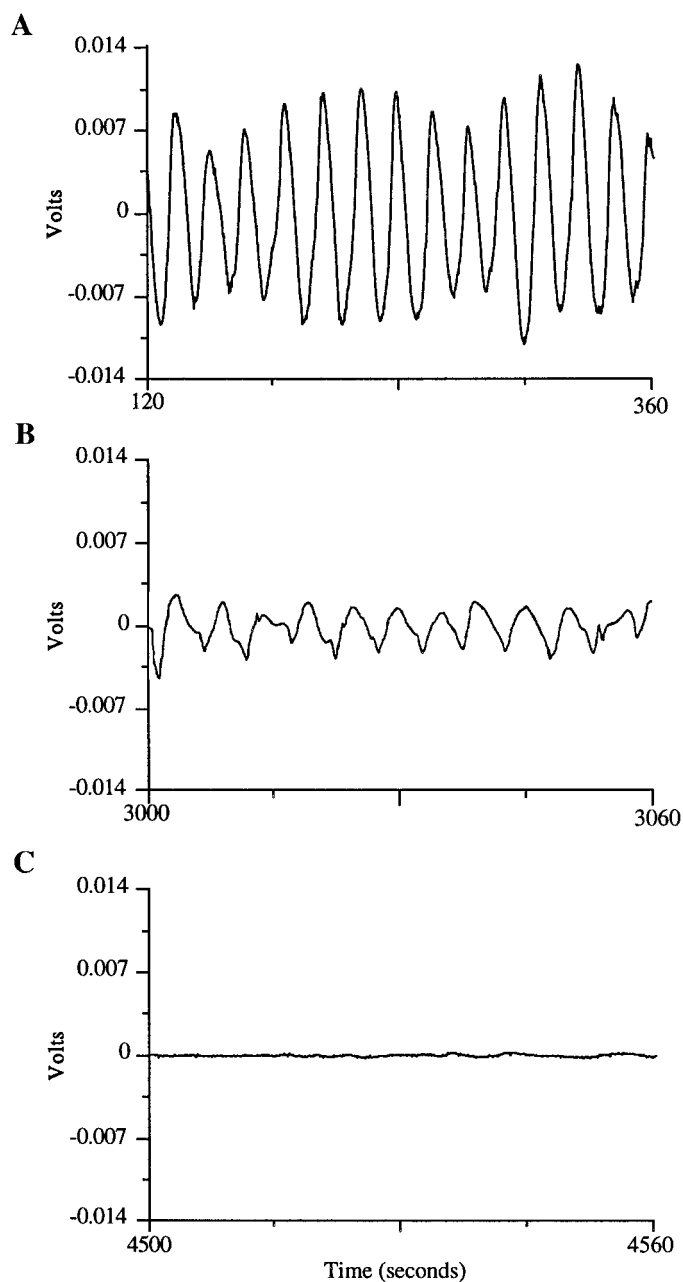


Fig. 1. Samples of electrical control activity (ECA) recordings from same animal at different time points during study. Baseline recording is shown in A. After 35 min (at 3,000 s of study time) of ischemia (B), frequency and amplitude of ECA signal are decreased. After 60 min of ischemia (4,500 s of study time), ECA signal is no longer detectable (C).

Autoregressive (AR) spectral analysis was used to determine ECA frequency on a Power Macintosh (Apple Computer) running MATLAB software (The Mathworks). Frequency is expressed as mean cycles per minute (cpm) \pm SE. One-minute segments were analyzed continuously over the duration of the entire study. The use of AR spectral analysis provides an objective assessment of frequency, rather than simply counting peaks over a known time period, which is subject to observer variability. Another major advantage of AR spectral analysis is that it can be used to examine short segments of recordings (1 min) rather than the longer segments (5 min) required by other analysis methods [such as

Fast Fourier Transformation (FFT); Ref. 4]. Additionally, AR spectral analysis can identify more than one frequency occurring within a single recording. Tachyarrhythmias were defined as those frequencies greater than two standard deviations higher than baseline ECA ($18.2 + 4.6 = 22.8$ cpm). Statistical analysis was performed using paired Student's *t*-test with significance defined as $P < 0.05$.

RESULTS

ECA recordings at baseline and at different time points during ischemia from a single study are shown in Fig. 1. ECA frequency fell from 18.2 ± 0.5 cpm at baseline to 12.2 ± 0.9 cpm ($P < 0.05$) after 30 min of ischemia and was undetectable by 90 min of ischemia in all animals. Tachyarrhythmias were recorded in at least one channel in 11 of 20 animals (55%) after various lengths of ischemia. These arrhythmias were noted to begin as early as 25 min after ischemia was induced (average time of onset 33.9 ± 1.9 min into ischemia) and lasted from 1 to 48 min (mean duration 14.3 ± 4.0 min). Frequencies ranged from 25 to 50 cpm. However, these tachyarrhythmias were not constant in frequency and could vary by as much as 20 cpm in one animal during a single episode. The characteristics of the tachyarrhythmias are shown in Table 1.

A typical tachyarrhythmia sequence is demonstrated in Fig. 2. The ECA during the baseline recording period is ~ 17 cpm. Ischemia is induced at 1,600 s. The frequency and amplitude decrease until after 3,600 s, at which time a faster rhythm is noted. The tachyarrhythmia continues for 15 min, at which time the ECA becomes undetectable. The running AR plot for the data presented in Fig. 2 is shown in Fig. 3. The abrupt end of an arrhythmia with reversion to a rhythm characteristic of ischemia is shown in Fig. 4. Another important characteristic of these tachyarrhythmias is that they were not always recorded in all four electrodes simultaneously, indicating that discrete segments of the ischemic loop of bowel were oscillating at different rates. Figure 5 demonstrates recordings obtained simultaneously from separate channels (labeled 1 and 2). Tachyarrhythmias are seen in both channels initially. However, the tachyarrhythmia in *channel 2*

Table 1. Characteristics of tachyarrhythmias

Animal	Length of Ischemia at Start, min	Duration, min	Frequency, cpm
1	28.7	23.3	50
2	25	6	40-50
3	35.8	14.7	25-35
4	44.2	6.6	25
5	30	6.7	35-45
6	35.7	1	35
7	33.7	5	35-40
8	37.8	48.4	35
9	44	18.7	40-45
10	26.5	11.7	30-40
11	31.8	15	30-50

Values are characteristics of tachyarrhythmias seen in 11 of 20 animals in study. Tachyarrhythmias started at 33.9 ± 1.9 min of ischemia and lasted 14.3 ± 4 min (means \pm SE). Frequencies of tachyarrhythmias were not constant and could vary by as much as 20 cycles per minute (cpm).

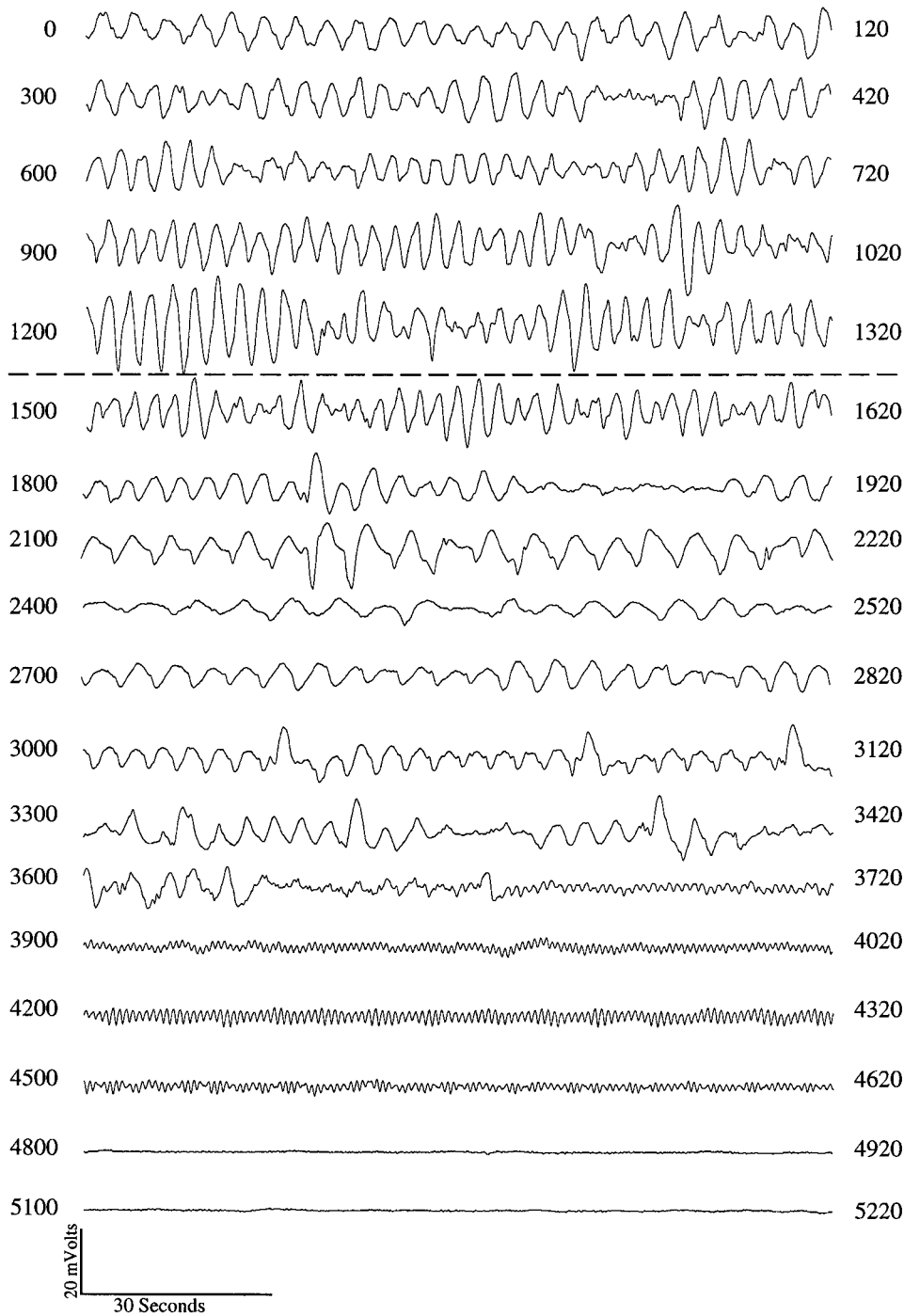


Fig. 2. Characteristic study progression of an animal exhibiting a tachyarrhythmia. Sequential time segments (2 min each) are displayed, and time points in seconds are shown for beginning and ending of each segment. ECA during the baseline recording period is ~17 cpm. Ischemia is induced at 1,600 s of study time (dashed line), and frequency and amplitude decrease until after 3,600 s of study time, at which time a faster rhythm is noted. Tachyarrhythmia continues for 15 min, after which the ECA becomes undetectable.

ends before the one in *channel 1* and reverts back to a rhythm characteristic of ischemic bowel. Figure 6 shows another set of recordings taken simultaneously from different channels. One segment of bowel experiences a tachyarrhythmia (*channel 1*), whereas another section 1 cm away appears to exhibit a bradyarrhythmia (*channel 2*). Of the 11 studies in which tachyarrhythmias were noted, 3 were seen in all channels, 3 were seen in more than one, but not all channels, and 5 were seen in one channel only. Even so, in all cases in which tachyarrhythmias were seen in multiple channels, the tachyarrhythmia in each channel ended at different

times (such as Fig. 5), such that there were still times when a tachyarrhythmia was recorded with one electrode while a rhythm characteristic of ischemic ECA was seen in the others. Figure 7 demonstrates differential frequencies during ischemic tachyarrhythmias. During the baseline period indicated, all three consecutive channels (*1, 2* and *3*) demonstrate ECA cycling at the same frequency, 18 cpm. During the period of tachyarrhythmia, however, the three adjacent electrodes record tachyarrhythmias of different frequencies by AR, indicating that the sections of bowel are oscillating at different rates.

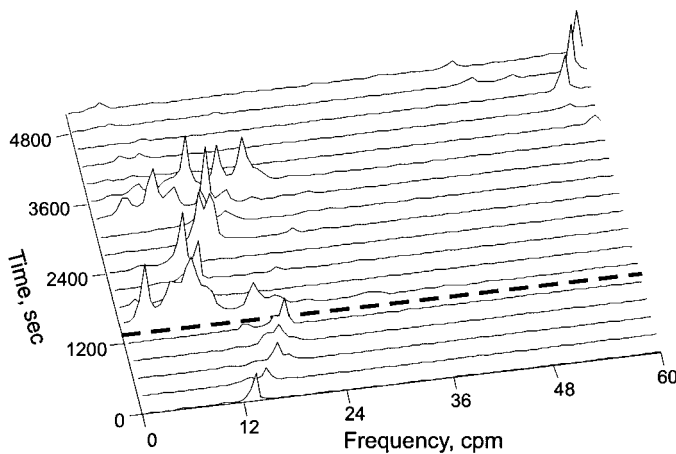


Fig. 3. Autoregressive (AR) spectral analysis. Corresponding AR graphs are shown for time points in Fig. 2 with frequencies of 12–15 cpm during baseline recording and 50 cpm during arrhythmia (seen after 3,600 s of study time).

DISCUSSION

We have shown that acute intestinal ischemia induces tachyarrhythmias that can be recorded using serosal electrodes. Although there is a wide variation in frequency and duration (Table 1), the use of AR spectral analysis reveals that they are relatively common, occurring in 11 of 20 (55%) of the animals in the study.

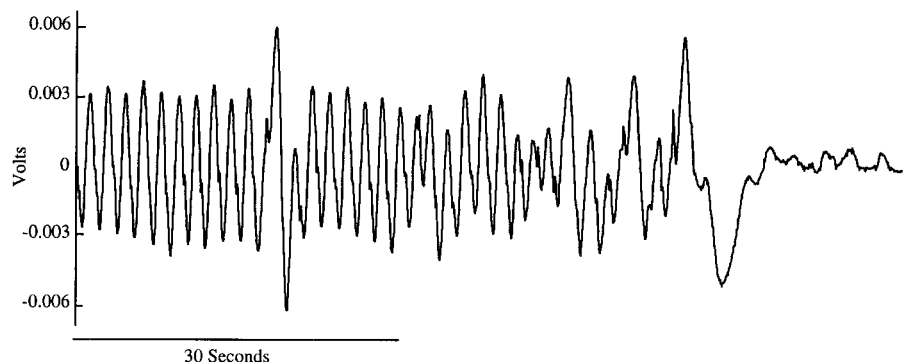
Although the phenomenon of tachygastrias and gastric tachyarrhythmias recorded with both serosal and cutaneous electrodes is quite common and accepted, intestinal tachyarrhythmias have not been previously reported (14). This is the first demonstration of small bowel electrical tachyarrhythmias of any kind. Fich and colleagues (9, 10) reported late postprandial rapid frequency (19–24 cpm) intraluminal pressure waves in the canine ileum accompanied by a one-to-one ratio of spike bursts and circular muscle layer contractions but noted that the ileal slow wave, or ECA, persisted at the normal frequency of 13–15 cpm. Another study (22) reported uncoordinated interdigestive myoelectric complexes in the small intestine in a patient with chronic nausea and vomiting but was unable to record ECA due to its small amplitude.

Within each segment of small bowel, the ECA is entrained by a proximal pacemaker. These pacemaker

cells pace a segment of smooth muscle cells that are connected by gap junctions or nexi. The organization of these syncytia of smooth muscle cells is such that there are segments of bowel entrained by a pacemaker cell arranged in a series of plateaus. The ECA frequency decreases in each successive (aboral) plateau, but within the plateau the ECA frequency is constant and determined by the proximal pacemaker (8). Although the exact mechanism of this phenomenon is still debated, it is clear that this mechanism is somehow disrupted in ischemic bowel, because the tachyarrhythmias recorded do not originate from all segments of the ischemic loop of bowel, as evidenced by the fact that they were not seen in all four electrodes simultaneously (Figs. 5–7). In fact, in some instances different arrhythmias were recorded simultaneously in separate channels (Fig. 7). We hypothesize that this is due to a “decoupling” of the smooth muscle cells. Ischemia has been shown to decrease coupling in cardiac myocytes due to increased deoxy stearic acids (6). Thus, in intestinal ischemia, separate segments of the decoupled ischemic bowel may exhibit different rhythms despite their close proximity. This phenomenon would most probably go unnoticed without the aid of AR spectral analysis. In fact, the occurrence of some of the tachyarrhythmias themselves would not be identified without the use of AR spectral analysis. Other analysis techniques, such as FFT spectral analysis, require at least 5 min of stable rhythm to determine spectral frequency (4), whereas some of the tachyarrhythmias last for only a short time interval. Thus the ability of AR analysis to analyze short segments of data enables the identification of more of these tachyarrhythmias than would be possible with visual or FFT analysis.

After the induction of ischemia, the ECA decreases in amplitude and frequency. This characteristic signal change is the first sign of ischemia and always occurred before the tachyarrhythmias. Because the tachyarrhythmias were only seen after a period of ischemia (never during baseline recordings), we believe they are pathognomonic for intestinal ischemia when they occur, although not a frequent early sign. This study utilized serosal electrodes to record the ECA signal and the intestinal arrhythmias. Obviously, this is an invasive means of detection. However, we have been able to

Fig. 4. Abrupt ending of a tachyarrhythmia and reversion back to a rhythm characteristic of ischemia.



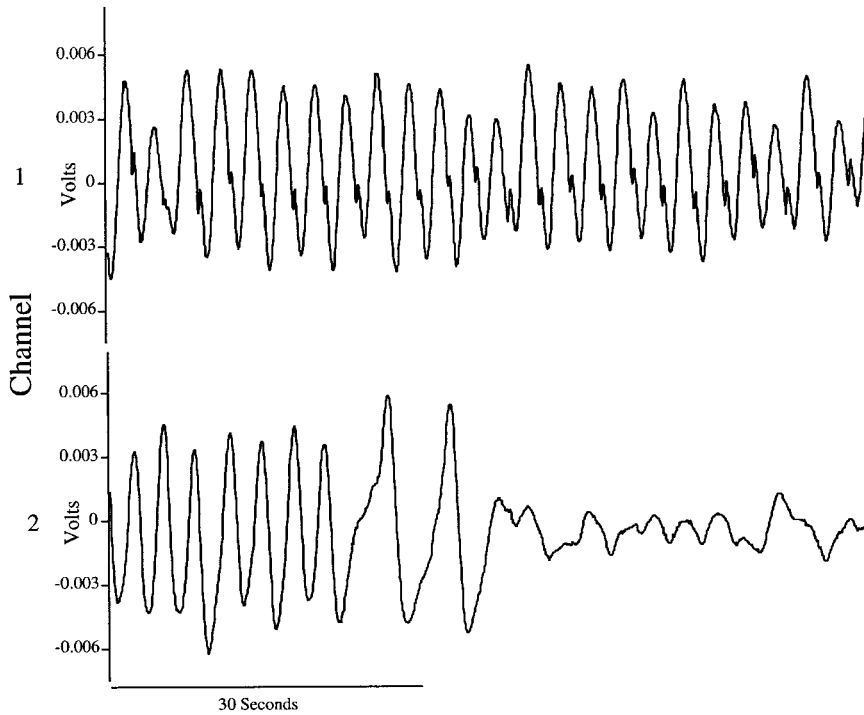


Fig. 5. Tracings recorded simultaneously from separate channels. Tachyarrhythmias are seen in both channels for some time, but *channel 2* tachyarrhythmia ends before *channel 1* tachyarrhythmia and reverts back to a signal characteristic of ischemic bowel.

utilize superconducting quantum interference devices (SQUIDs) to noninvasively detect the frequency and amplitude changes in small bowel ECA during mesenteric ischemia in animal studies (1, 2, 3, 12, 16). If intestinal tachyarrhythmias can be detected using SQUID magnetometers, then we would have yet another signal marker characteristic of ischemia to noninvasively identify mesenteric ischemia. The specificity of such an indicator would be high, because these tachyar-

rhythmias have been recorded only during episodes of ischemia. The level of sensitivity remains to be seen, but the fact that arrhythmias occurred in 55% of the animals in this study is promising for noninvasive detection of mesenteric ischemia. SQUIDs have also been used to record normal ECA in >40 human volunteers (15, 17, 19). Currently, we are investigating whether tachyarrhythmias can be recorded using the SQUID magnetometers. If detecting tachyarrhythmias

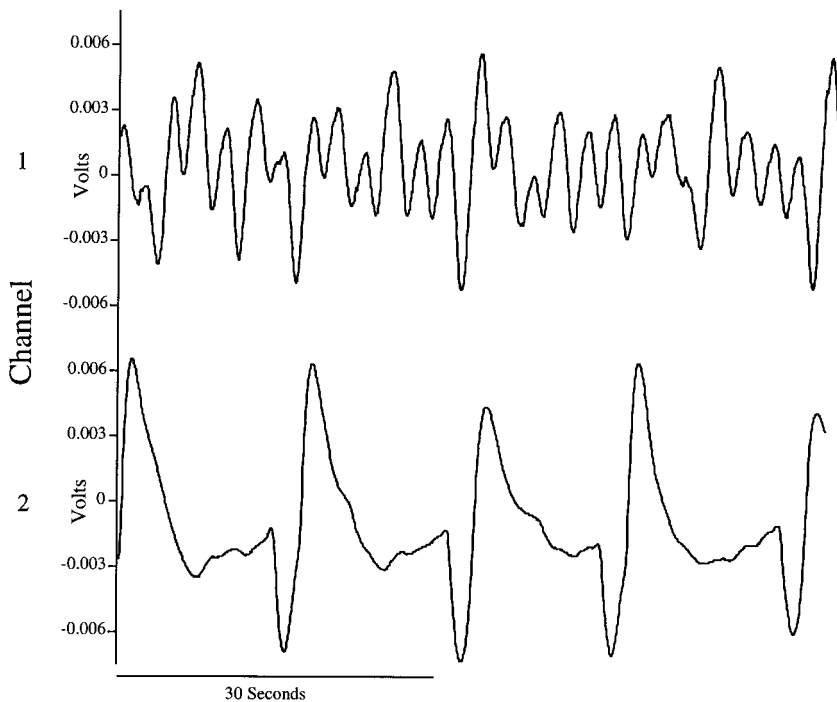


Fig. 6. Recordings obtained simultaneously from separate channels. In this case, completely different arrhythmias are seen at same time points. One segment of bowel experiences a tachyarrhythmia (*channel 1*), and at same time another adjacent section experiences a bradyarrhythmia (*channel 2*).

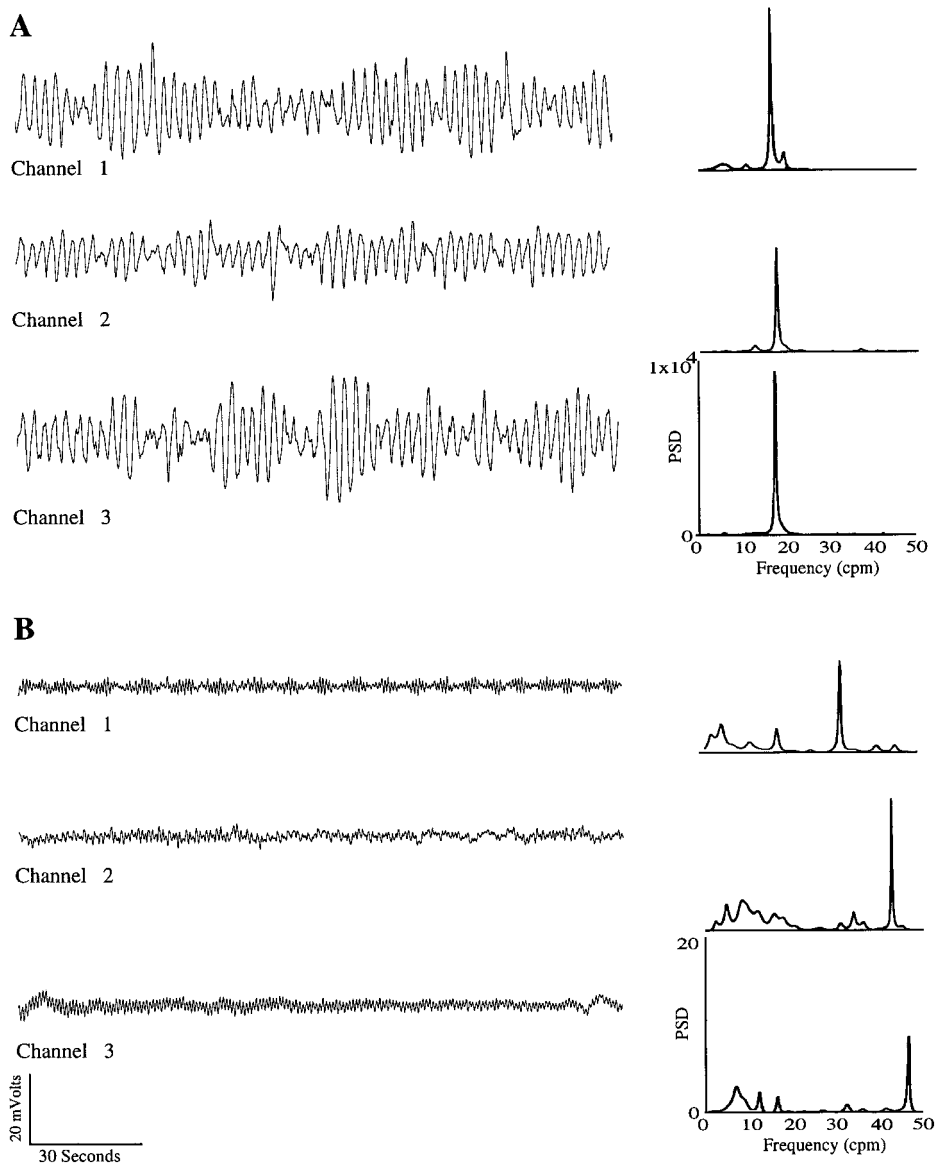


Fig. 7. Differential frequencies during ischemic tachyarrhythmias. During baseline period indicated (A), all 3 consecutive channels (1, 2, and 3) demonstrate ECA cycling at same frequency, ~18 cpm. During period of tachyarrhythmia (B), however, 3 adjacent electrodes record tachyarrhythmias of different frequencies by AR, indicating that sections of bowel are oscillating at different rates.

using SQUIDS is possible, then this method of detecting mesenteric ischemia early in its course may lead to a better prognosis in these critically ill patients.

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