

Textured collagen, a hemostatic agent

A pilot study

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The hemostatic properties of a new form of bovine collagen were observed on 25 dental patients. Early in the investigation it became apparent that pain, swelling, and trismus were reduced and healing was accelerated.

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The control of bleeding has been a challenge from the earliest days of surgery. Today, ligation and suture remain the most convenient methods of hemostasis for most situations. However, on certain occasions problems remain, particularly in large oozing surfaces or when access is poor.

Under the influence of Hippocrates, cauterization was the popular method of hemostasis for many centuries. Early in this century, where ligation was impracticable, various materials such as muscle,¹ fat, and fascia were used. The substantial collagen content of these tissues, especially muscle and fascia, provide an autologous hemostatic wound dressing. In 1915 Grey,² used sterilized washed patches of sheep's blood fibrin. Harvey³ improved on this by mincing the fibrin and compressing it into thin sheets. In 1940 Bering⁴ developed a fibrin foam from dried human plasma. The first true fabric designed for hemostasis, presented by Yackel and Kenyon⁵ in 1942, was oxycellulose, produced by treating cotton gauze with nitric acid. In 1945 Correll et al.⁶ introduced a gelatin foam. This was improved by Jenkins and Clarke,⁷ who soaked this foam in a thrombin solution.

The 1967 report of Battista et al.⁸ on Avitine microcrystalline powder (Avicon Inc., Fort Worth, Tex.) demonstrated that commercially available collagen has excellent hemostatic properties. However, it is expensive and difficult to handle with surgical gloves and instruments. The fine powder fibers readily become airborne and migrate beyond the operative site. One year later Chvapil and Rolusa⁹ introduced a new form of lyophilized collagen sponge. In 1985 Stein et al.¹⁰ demonstrated the use of a porous colla-

gen sponge to control bleeding from oozing palatal periodontal donor sites.

Eckmeyer et al.¹¹ provided a further refinement by processing purified collagen into long fibers that were then fabricated into nonwoven pads of various sizes. This type of collagen is now available as Hematex (BIOPLEX Corp., Montvale, N.J.). The pads are readily cut and tailored to any shape, according to the particular environment. Hematex was chosen as the focus of this study because of its features. It is composed of native collagen fibers, as is the potent Avitine powder, but is more coherent, to prevent migration or aspiration. It has the convenience and purity of sponges but without the prominent porosity.

Various other configurations are now in preparation such as a loose fiber form for office and hospital use.

Hematex collagen is derived from bovine Achilles tendon by a complex chemical process. The product is available in double-sheathed sterile packs, free from noncollagenous proteins, toxic heavy metals, and glycosaminoglycans. It is also pyrogen free, nontoxic, and nonirritating. Chvapil et al.¹² pointed out that collagen can be mildly allergenic. However, Bell et al.¹³ found that when the animal collagen was highly purified, the problems of allergenicity and unwanted tissue reaction did not arise.

Except for size, Hematex collagen is identical to Novacol (BIOPLEX Corp.), which is marketed to hospitals worldwide for use in surgery, thoracic surgery, trauma surgery, and most recently neurosurgery.¹⁴ The same product is used in hospitals in the United States under a different trade name.

Another collagen product derived from porcine skin has been used by Mitchell and Lamb,¹⁵ who successfully closed off 30 oroantral communications. In

another study Mitchell¹⁶ used porcine collagen in 37 cases to cover areas in the mouth deprived of mucosa.

Although much work on collagen has been reported in the literature, there are presently few if any contemporary studies of its use in dental extractions with their bone and soft tissue components.

The purpose of this investigation was to observe for the first time the efficacy of Hematex collagen in the control of dental bleeding and any related phenomena.

Evidence now exists that collagen accelerates hemostasis at four levels:

- Stimulation of platelet adhesion, platelet aggregation and release reaction^{17, 18}
- Activation of Factor XII (Hageman factor) and possibly other factors¹⁹⁻²¹
- Mechanical tamponade by the structure that forms at the collagen-blood interface
- Release of serotonin

MATERIAL AND METHODS

Thirty-five consecutive patients undergoing various forms of dental surgery in a general dental practice were considered for the trial. Twenty-five were eventually selected. Ten patients were excluded because of underlying medical conditions (pregnancy, hypertension, thrombocytopenia), age less than 14 years, or inability to return the next day for review.

No patient eligible for the trial was unwilling to participate. A license to conduct clinical trials had been granted by the British Department of Health and Social Security.

Because this was a pilot study in which little was known of the outcome, no attempt was made to compare with an age-matched group. All treatments and observations were done by the same person. The limitations of such a system are accepted and recognized.

A comprehensive questionnaire was drawn up to evaluate the patients' medical and dental status, especially the level of periodontal disease (categorized as good, bad, or fair). Where necessary, this was followed by a brief medical examination. Attention was paid to current health, bleeding, or bruising problems in the patient, parents, siblings, and children. Details of any medication were noted.

All the surgical procedures were done with the use of a local anesthetic (2% lidocaine with 1:80,000 adrenaline). General anesthesia was not used in any patient. This was done to allow adequate time to observe the effect of Hematex collagen and to take appropriate conventional steps to deal with excessive bleeding that might occur. After the procedure a suitable piece of Hematex collagen was packed into

the resultant cavity. Light pressure with a gauze pad was applied to ensure coverage of all bleeding surfaces. The time for bleeding to cease was recorded. All patients were assessed the next day and, where possible, the next week.

The original aim of the study was to observe hemostasis. After the earliest cases it was clear that the material had other properties, and the study was redesigned to monitor these effects.

Observations made the next day included the status of the operative area; conditions elsewhere in the mouth; and pain, swelling, bruising, or trismus. Pain was assessed empirically. It was marked as painful if more than one dose of an analgesic had been taken. Unless contraindicated, aspirin products were suggested to the patient. This was deliberately done to challenge the coagulation mechanism. No firm guidelines were possible for degree of socket healing. A clinical judgment was made on the amount the socket caliber was reduced and the absence of inflammation. The patients were asked to report on the length of bleeding, including any blood-stained saliva after leaving the office. Trismus and swelling were judged on a subjective basis. No attempt was made to quantify them.

RESULTS (Table I) Effect on bleeding

It should be borne in mind that none of these cases were sutured, including eight involving surgical removals. Among the 24 patients whose operative bleeding time was recorded, only four (20%) bled for more than 2 minutes when treated with Hematex collagen. None of the patients undergoing surgical removals bled for more than 3 minutes. The average operative bleeding time was 1.82 minutes; the longest was 7 minutes. The average was 2.35 minutes for the 10 males and 1.73 for the 15 females.

Delayed bleeding or rebleeding occurred in five patients. One of them underwent a surgical removal and one (patient 18) had a frank abscess. All five had highly inflamed periodontal tissues. The conclusion can be made that, in the presence of inflammation, Hematex collagen functions but is less efficient.

Two patients had more than one site of bleeding. In patient 8, a 48-year-old woman, six teeth in two quadrants were extracted. Three sockets were treated with Hematex collagen; three were not. Treated sockets bled for 2 minutes whereas those untreated bled for 15 minutes. On day 1 examination showed healing at the treated sites but not at the untreated sites.

Patient 9 was a 38-year-old man who had one tooth with two discrete roots surgically removed. The larger

Table 1. Results of 25 cases treated with Hematex collagen

<i>Patient No.</i>	<i>Sex/age (yr)</i>	<i>No. of teeth (roots)</i>	<i>Operative bleeding time (min)</i>	<i>Pain, swelling, trismus</i>	<i>Day 1 healing</i>	<i>Periodontal status</i>
1	M/34	1	2	Swelling	None	Bad
2	M/47	1	2	None	Healing	Fair
3	F/40	1	5	None	Healing	Good
4	M/59	1	0.5	None	Healing	Fair
5	F/32	1	4	None	Healing	Good
6	F/45	1	1	None	Healing	Good
7	F/49	1	2	None	Healing	Good
8	F/48	3	2	None	Healing	Bad
9	M/38	1	N/A	None	Healing	Good
10	F/40	1	1	None	Healing	Good
11	M/37	1	7	None	None	Good
12	M/39	1	1	None	Healing	Good
13	F/15	1	1	None	Healing	Good
14	F/30	1	2	None	Healing	Good
15	F/15	1	1	None	Healing	Good
16	F/54	1	1	None	Healing	Good
17	M/20	1	2	Slight swelling	Healing	Good
18	M/58	1	2	None	Healing	Good
19	M/43	1	2	None	Healing	Good
20	F/42	1	Nil	None	Healing	Bad
21	M/66	1	1	None	Healing	Good
22	F/66	1	0.5	None	Healing	Fair
23	F/30	1	2	Pain	Healing	Good
24	F/34	1	0.5	Pain	Healing	Bad
25	F/33	1	3	None	Healing	Good

N/A, Not available.

socket, which was treated (the smaller was untreated), bled less and showed more healing on day 1.

In patient 19 a coagulation variable was known with certainty. The patient was a 38-year-old man who had previously had heart surgery. He was taking anticoagulant medication and had a prothrombin ratio of 2.2:1 when a third molar was surgically removed. In Western society the number of patients taking such medication increases each year; dental surgeons can expect more cases of bleeding from this cause.

Redding and Olive²² showed that a 10-point questionnaire was a better guide to potential bleeding than three routine tests (prothrombin time, activated partial thromboplastin time, and bleeding time). With this questionnaire, together with Hematex collagen, it should be possible for the dental practitioner to deal with most coagulation-compromised patients. In addition, for the inexperienced surgeon Hematex collagen is easy to use and will eventually become cheaper than suture materials.

Effect on pain

By the criteria used, all patients were remarkably pain free. Exceptions were patients 23 and 24, women aged 30 and 34 years, respectively. The reason for this is not known.

Effect on healing

Miller²³ stated that in addition to its now known hemostatic properties, collagen fibers provide extracellular support for mineralized and nonmineralized tissues and influence the migratory differentiation and biosynthetic activities of cells.

The effect of Hematex collagen on healing is difficult to quantify, but I was impressed by the state of sockets on day 1 (the day after extraction). In two cases (8 and 9) a direct comparison between treated and untreated sockets was possible in the same patient. In four of the eight surgical cases (9, 13, 17, and 25) signs of infilling were present on day 1.

Effect on resorption

In two cases (2 and 10) partial immediate dentures were supplied. It was possible to see that no resorption had occurred by day 7. In case 10 models were made preoperatively and again at 14 days postoperatively. No dimensional changes were seen.

Effect on swelling and trismus

Marked swelling appeared in one case only (case 1), a grossly infected mouth. Slight swelling appeared for one day in case 17, a difficult lower third molar. In this case and in surgical cases 9, 14, 19, and 25, I firmly

believe that without Hematex some of these patients would have had trismus. It may be that collagen successfully blocks out dead spaces within bone.

Other effects

In patient 21, originally excluded from the study because of hypertension, an oroantral fistula developed after the removal of an upper molar. With Hematex collagen closure of the fistula was secured. This is in keeping with known properties of collagen, which have been reported elsewhere.¹⁵ No evidence of allergic or irritant phenomena was found in this study.

CONCLUSION

This pilot study revealed that textured collagen has powerful hemostatic properties in the mouth, confirming what is known about its behavior in other areas of the body. Compared with traditional suturing, textured collagen is simple to use, requiring only one instrument. Recently oral surgeons have been compelled to rethink their sterilization standards. It follows that cross-infection is easier to control if fewer instruments are in use. No side effects were observed.

Other benefits, such as improved healing, pain control, and preservation of alveolar bone, may exist. Further studies are planned to assess these properties more critically. It is not now known whether textured collagen can be used for established dental bleeding.

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