Spring 2005

JOURNAL OF BIOMEDICAL THERAPY

Integrating Homotoxicology and Mainstream Medicine

Homotoxicological adjunct in cancer treatment

Traumeel in stomatitis

Antihomotoxic remedies in canine mammary tumors

Official publication of SOHNA
Luffeel/BHI Hayfever Nasal Spray’s efficacy in the treatment of seasonal allergic rhinitis was confirmed in a study comparing it to a cromolyn sodium nasal spray. After 6 weeks, this study concluded that, for the treatment of hay fever, the homeopathic nasal spray was as efficient and well tolerated as the conventional therapy with cromolyn sodium.1)

Luffeel/BHI Hayfever Nasal Spray:
- Effectively reduces nasal and ocular allergic symptoms
- Is appropriate for long-term treatment
- Is suitable at all ages (including children, pregnant and nursing women)

Luffeel/BHI Hayfever Nasal Spray is a complete remedy which can be used for prevention or treatment, alone or in conjunction with other remedies such as Psorinoheel/Sorinoheel and Hepar compositum.

This issue is dedicated to the adjuvant treatment of cancer patients. The subject of treating cancer patients with biological therapy has always been a controversial one, with colleagues writing about charlatans taking advantage of desperate patients, and making claims which are far fetched as far as cancer cures are concerned.

This line of thinking is further fueled by the interactions some phyto-therapeutic agents have with cancer treatments, which result in the condemnation of all biological treatments, even though in microdose treatment, such as used in Homotoxicology, no interactions have been observed. The current multicentral study on the treatment of stomatitis in children, which expands on the Traumeel study published in this issue, is a good example of this. While there may be some practitioners exploiting the desperation of this group of patients, for the most part, biological therapy, when applied in the right circumstances by informed practitioners, can be of tremendous benefit to the cancer patient. It is thus a pity that so few opportunities exist to work as a holistic team in the treatment of this complex disease.

Cancer has a multifactorial and complex etiology, with environmental chemicals, immune dysfunction and poor DNA repair processes being only a few elements which are indicated in the initiation and development of the cancerous process. In addressing the cancer patient, care must thus be given to multiple aspects such as nutritional status, toxin ingestion and detoxification abilities as well as certain stressors such as psychological stress and coping mechanisms.

Biological therapy can be used in all stages of cancer, from the prevention to the support during conventional cancer treatments such as chemotherapy and radiation. A major benefit of biological therapy is treating the patient in remission, where care can be given to the detoxification of possible initiators of the cancerous process as well as in the aftermath of chemotherapy substances. Optimizing the greater defense system in order to prevent recurrence is another aim with the patient in remission. Even in the terminal stage, the application of anti-homotoxic medicine can be of tremendous help to improve the quality of life. Support during chemotherapy is another area of interest, and the topic of the study published in this journal where Traumeel has been successfully employed in an RCT for the treatment of chemotherapy-induced stomatitis. It is also a sad fact that we also see an increase of cancer in our animals, and veterinarians need to inform themselves more about this disease. The study dealing with anti-homotoxic treatment for tumors in dogs is an example of the excellent contribution our veterinary colleagues are making to the study of Homeotoxicology.

Lastly we are expanding the column “In Your Practice” where case studies will be presented. In this issue, we publish a case of asthma, written by Dr. Maureen Horne-Paul who practices in Canada. We would like to invite all practitioners with interesting cases to write them down and submit them for publication (photographs are welcome).
The International Society of Homotoxicology, which was founded in Germany in 1961 by Dr. Hans-Heinrich Reckeweg, the inventor of Homotoxicology and genius modernizer of classical homeopathy, has for long been a small German-oriented society. However, with increasing interest in Homotoxicology in all parts of the world, the Society's focus has shifted to include new physicians and healthcare professionals interested in the concept of Homotoxicology.

To be better prepared for this task, the presidency of the Society decided to create the position of a Secretary General in the Society. In July 2004, Dr. Josef A. Hoffmann, MD, BSc, took over the new position of Secretary General for the International Society of Homotoxicology. Dr. Hoffmann is a physician and biologist who trained in internal medicine, then worked for three years at the German Cancer research centre, followed by five years of clinical experience in internal medicine and cardiology, before he entered the pharmaceutical industry in 1988. He served in leading positions in medical departments: four years as the Medical Director of Upjohn and seven years as Senior Head of the Medical and Scientific Department Therapeutics in Pharmacia Germany. His broad experience in all aspects of medical and scientific demands ensures that he will support our Society to validate the scientific basis of Homotoxicology.

The demand for biological therapy is already tremendous (in Germany over 75% of the population, asked in a representative survey, wants to be treated with natural medicine) and will continue to grow. Events like the withdrawal of anti-inflammatory drugs such as rofecoxib for symptomatic treatment of arthritis will surely add to this demand.

Although Homotoxicology is amongst the best researched modalities in natural medicine, further studies are needed to prove the efficacy and the working mechanisms of our well tolerated drugs. This is one of the International Society's aims, to bring together experts from various countries to discuss the possibilities for scientific projects, find a sponsor and perform such projects in the best mode according to the highest standards of the pharmaceutical industry worldwide.

For this purpose, the International Society is proud to offer a yearly prize. The winner receives the Hans-Heinrich Reckeweg Award for scientific work done with fundamental, theoretical and/or practical significance for complex homeopathy (anti-homotoxic medicine) in the following areas:

- Fundamental contribution to the scientific justification of complex homeopathy (anti-homotoxic medicine)
- Practical application of homeopathic combination preparation therapy (anti-homotoxic therapy) in clinic and/or practice (human medicine)
- Therapeutic work in the field of biological veterinary medicine

The amount awarded for the first prize is 10,000 € (Euros). The Society also awards a second prize for results arising from clinical, practical or fundamental research that invites further investigation. This Hans-Heinrich Reckeweg promotion Prize is rewarded with 5,000 €.

Potential applicants should submit two copies of their manuscript in English or German in a form suitable for publication. The requirements are outlined in the manuscript guidelines (available upon request). The deadline for submission is May 31st of every year. The manuscripts must be submitted to the International Society of Homotoxicology, PO Box 100 264, 76483 Baden-Baden, Germany. Conditions of entry may be requested through e-mail: info@homotox.de
Cancer patients have special needs in terms of detoxification and drainage. Firstly, it is important to notice that detoxification and drainage put considerable strain on the organism. Caution should thus be exercised in very ill patients. Secondly, one does not want to detoxify and drain patients receiving chemotherapy, as it will impair the efficacy of the chemotherapy if it is actively drained from the tissues at the time of administration.

Drainage is thus best delayed until about six weeks after the last chemo dose. This is an arbitrary time span, as the pharmacokinetics of each chemotherapy compound is dependent on a number of factors including age, gender and weight of the patient, genetics, concomitant disease, absence of co-factors of the various detoxifying enzymes, and also the simultaneous intake and exposure to other endogenous and exogenous homotoxins.

In general, it can be said that the elderly and females (higher fat content and also slower detoxification through the P450) and overweight patients detoxify slower and that in these cases, one should detoxify a bit longer, especially if there is a presence of other homotoxins.

### Protocol for detoxification and drainage of cancer patients

#### Step 1: Preparation and support of the detoxifying organs (weeks 1-6)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Compositum</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>Hepar compositum</td>
<td>1 oral vial 3 times per week</td>
</tr>
<tr>
<td>Kidney</td>
<td>Solidago compositum or Reneel</td>
<td>1 oral vial 3 times per week or 1 tablet 3 times per day</td>
</tr>
<tr>
<td>Matrix</td>
<td>Thyreoidea compositum or Funiculus umbilicalis suis-Injeel and Pulsatilla compositum (especially if the patient had cortisone)</td>
<td>1 oral vial 3 times per week</td>
</tr>
<tr>
<td>Cellular</td>
<td>Glyoxal compositum</td>
<td>1 oral vial 3 times per week</td>
</tr>
<tr>
<td>Orthomolecular support</td>
<td>Multivitamin/trace element/mineral supplement Especially add sulphydryl supporting compounds such as N-Acetyl Cysteine (NAC)</td>
<td>Dose as per preparation Dose NAC 500 mg 3 times daily</td>
</tr>
</tbody>
</table>

#### Step 2: Detoxification and drainage (weeks 6-12)

<table>
<thead>
<tr>
<th>Organs</th>
<th>Compositum</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver and gut</td>
<td>Detox-Kit: Nux vomica-Homaccord</td>
<td>30 drops of each, in 1 liter of non-sparkling water, to be taken as small sips throughout the day</td>
</tr>
<tr>
<td>Kidney and biliary tract</td>
<td>Berberis-Homaccord</td>
<td></td>
</tr>
<tr>
<td>Lymph drainage (matrix)</td>
<td>Lymphomyosot/Lyphosot</td>
<td></td>
</tr>
<tr>
<td>Deep lymph drainage</td>
<td>In older patients (over 45), start with Galium-Heel/Galium-Heel Comp. first instead of Lymphomyosot/Lyphosot for these six weeks</td>
<td>10 drops three times per day or 1 oral vial 3 times per week</td>
</tr>
<tr>
<td>Cellular detoxification and drainage</td>
<td>Coenzyme compositum and Ubichinon compositum or Ubicoenzyme</td>
<td>1 tablet 3 times per day or 10 drops 3 times per day or 1 oral vial 3 times per week</td>
</tr>
</tbody>
</table>

If the patient is very toxic or in a group which detoxifies very slowly, repeat steps one and two.

#### Step 3: Draining the matrix (weeks 12-36)

<table>
<thead>
<tr>
<th>Compositum</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphomyosot/Lyphosot</td>
<td>20 drops twice per day or 1 tablet 4 times per day or 1 oral vial 4 times per week</td>
</tr>
</tbody>
</table>

Note: This same protocol can be used to detoxify non-cancer patients as prevention for cancer in order to drain the body of potentially carcinogenic toxins.
The combination of biological and conventional medicine in cancer patients is often an area of controversy, as many oncologists are weary of mixing treatments which may have interaction with the chemotherapy. This is not unfounded, as a number of phytotherapeutic agents are known to interact with chemotherapy drugs, either by slowing the metabolism, preventing the action of the agent on the cancer cell or by increasing the toxicity. One such substance, which slows down the P450 to the point of irreversible damage is, for instance, grapefruit juice. Other phytotherapeutic agents have a known effect on the coagulation system, which also may put the patient at risk. It is thus wise for practitioners using phytotherapy to inform themselves accordingly. (1-3)

Recent surveys have shown that up to 80% of all cancer cases use concomitant biological and conventional therapies. (2) Microdose therapy (homeopathic remedies) is not thought to have any interaction with conventional chemotherapeutic agents. For instance, an extension of the study we publish in this issue is a multicentric trial currently being done on Traumeel by the Children's Oncology Group. (1)

Support with anti-homotoxic medicine does not only imply detoxification as it has been mentioned before, but should be aimed at diminishing the effect of the chemotherapy on the healthy cell. The various groups of chemotherapy agents have different effects on the system. The most common side effects are seen in the fast dividing tissues such as the mucosae, the bone marrow, the gonads, and the hair follicles. As for nausea and vomiting, biological medicine can lend tremendous support to the patient without adding to the toxicity of the treatment regime. Fatigue is one of the most common side effects of chemotherapy. This is reported by the patients to be one of the most debilitating symptoms. It is usually very bad (the “nadir”) a week to ten days after a chemotherapy treatment and coincides with a drop in the white cell count (WCC). The fatigue can continue for six months after treatment.

### Support of the patient during chemotherapy or radiation

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### Side effect | Commonly used therapy regimes responsible | Anti-homotoxic treatment | Dose
---|---|---|---
Fatigue | All, including radiotherapy (especially for brain tumors) | China-Homaccord, Aletris-Heel, Ginseng compositum* | 10 drops 3 times daily or 1 oral vial 3 times weekly 1 tablet 3 times daily 10 drops 3 times daily 1 oral vial daily
Bone marrow suppression | ABVD, AC, BEP, CHOP, CMF (less frequent), FEC, MIC, MMM, PCV, Radiotherapy (total body irradiation) | Tonsilla compositum or Medulla ossis suis-Injeel and Glandula suprarenalis suis-Injeel | 1 oral vial 3 times weekly
Fever and chills | PCV (children), ABVD, BEP (with an allergic reaction) | Aconitum-Homaccord | 10 drops every 15 min. for 8 doses or 1-3 oral vials daily, then 10 drops 3 times daily or 1 oral vial daily
### Digestive system

<table>
<thead>
<tr>
<th>Nausea and vomiting</th>
<th>Doxorubicin, AC (severe), BEP, CMF, FEC (severe), MIC (severe), MMN, PCV (gets better through course)</th>
<th>Nux vomica-Homaccord</th>
<th>Ginger tea or Ginger tablets</th>
<th>10 drops up to five times a day or 1-3 oral vials daily (start on the day before) 2 tablets three times a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>ABVD, CMF, FEC</td>
<td>Diarrheel/Areel</td>
<td>1 tablet 3-5 times daily</td>
<td></td>
</tr>
<tr>
<td>Stomatitis</td>
<td>ABVD, AC, CHOP, FEC</td>
<td>Traumeel</td>
<td>1 oral vial in water 5 times daily (see study on p. 8)</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>PCV</td>
<td>Nux vomica-Homaccord</td>
<td>10 drops 3 times daily or 1 oral vial weekly</td>
<td></td>
</tr>
<tr>
<td>Mouth ulcers</td>
<td>ABVD, AC, CHOP, FEC</td>
<td>Gastricumeel/Astricumeel</td>
<td>1 tablet 3 times daily</td>
<td></td>
</tr>
</tbody>
</table>

### Skin and hair

<table>
<thead>
<tr>
<th>Temporary hair loss (alopecia)</th>
<th>Doxorubicin, AC, CHOP, CMF, FEC (can be complete, head and body)</th>
<th>Cutis compositum or Funiculus umbilicalis suis-injeel</th>
<th>1 oral vial 3 times weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burns</td>
<td>Radiotherapy</td>
<td>Causticum compositum</td>
<td>10 drops 3 times daily or 1 oral vial 3 times per week, start two days before radiation</td>
</tr>
</tbody>
</table>

*Caution: Contains Ginseng in mother tincture thus, do not use with anthracyclines (e.g. Mitozantrone), alkalyting agents (e.g. Cyclophosphamide, Dacarabazine), and podophyllum (epipodophyllins, e.g. Etopside) agents.

### REGIMES:

- **ABVD**: Adriamycin, Bleomycin, Vinblastine, Dacarabazine (used for Hodgkin’s lymphoma)
- **AC**: Adriamycin (Doxorubicin), Cyclophosphamide (used for breast cancer)
- **CMF**: Cyclophosphamide, Methotrexate, 5-FU (5-Fluorouracil) (used for breast cancer)
- **FEC**: 5-FU, Epirubicin, Cyclophosphamide (used for breast cancer)
- **MMM**: Mitozantrone, Mitomycin C, Methotrexate (used for breast cancer)
- **BEP**: Bleomycin, Etopside, Platinum (used for testicular cancer)
- **CHOP**: Cyclophosphamide, Doxorubicin hydrochloride (Adriamycin), Vincristine (Oncovin), Prednisolone (used for non-Hodgkin’s lymphoma)
- **MIC**: Mitomycin C, Isosamamide, Cisplatin (used for non small cell lung cancer)
- **PCV**: Procarbazine, Lomustine (CCNU), Vincristine (used for brain tumors)

### References:

3. Natural Medicines comprehensive database. At www.naturaldatabase.com
A randomized, controlled clinical trial of the homeopathic medication
Traumeel S in the treatment of chemotherapy-induced stomatitis in children undergoing stem cell transplantation

Background: Stomatitis is a common consequence of chemotherapy and a condition for which there is little effective treatment. Although the management of patients with other chemotherapy-related toxicities has improved in recent years, the incidence of stomatitis is increasing because of more intensive treatment and is often a dose limiting factor in chemotherapy. The authors assessed the efficacy of a homeopathic remedy, TRAUMEEL S®, in the management of chemotherapy-induced stomatitis in children undergoing bone marrow transplantation.

Methods: A randomized, placebo-controlled, double-blind clinical trial was conducted in 32 patients ages 3-25 years who had undergone allogeneic (16 patients) or autologous (16 patients) stem cell transplantation. Of the 30 evaluable patients, 15 were assigned placebo, and 15 were assigned TRAUMEEL S® both as a mouth rinse, administered five times daily from 2 days after transplantation for a minimum of 14 days, or until at least 2 days after all signs of stomatitis were absent. Stomatitis scores were evaluated according to the World Health Organization grading system for mucositis.

Results: A total of five patients (33%) in the TRAUMEEL S® treatment group did not develop stomatitis compared with only one patient (7%) in the placebo group. Stomatitis worsened in only 7 patients (47%) in the TRAUMEEL S® treatment group compared with 14 patients (93%) in the placebo group. The mean area under the curve stomatitis scores were 10.4 in the TRAUMEEL S® treatment group and 24.3 in the placebo group. This difference was statistically significant (P < 0.01).

Conclusions: This study indicates that TRAUMEEL S® may reduce significantly the severity and duration of chemotherapy-induced stomatitis in children undergoing bone marrow transplantation.

Keywords: TRAUMEEL S®, stomatitis, mucositis, autologous, allogeneic, stem cell transplantation, bone marrow transplantation, randomized, placebo-controlled, homeopathy, complementary medicine.

Stomatitis occurs commonly as part of general inflammatory damage to the mucous membranes in patients receiving chemotherapy or radiation therapy to the oropharyngeal region. The overall incidence of reactive stomatitis is about 40%. However, it is particularly common in patients receiving 5-fluorouracil (5-FU) treatment and is even more common in those undergoing radiation therapy for malignancies of the head and neck, in which approximately 80% of patients are affected. In patients undergoing bone marrow transplantation (BMT), the incidence of stomatitis reached 95%.

The mechanism of development of stomatitis is primarily cytotoxic, although neutropenia, periodontal pathology, poor oral hygiene, poor nutritional status, and infections also contribute to the condition. Morphologic characteristics can vary from slight erythema and edema of the oral mucosa to severe, focal, or widespread ulceration, bleeding and exudation. In addition to pain and discomfort, loss of the mechanical barrier together with the large surface of necrotic mucosa and neutropenia can lead to secondary local infections, sepsis, and even life-threatening systemic infections. Severe cases of stomatitis often necessitate the interruption of chemotherapy treatment or dose reduction and may affect patient compliance with further treatment. Compared with other chemotherapy-related toxicities, such as myelosuppression, the incidence of mucositis and the significance of its toxicity is increasing. Consequently, oral mucositis is becoming the most common dose-limiting toxicitiy of chemotherapy.

The current treatment of patients with stomatitis is essentially symptomatic. This includes stringent oral hygiene, avoiding irritative and abrasive foods, good oral and dental care, and the use of bland rinses, topical anesthetics, and systemic analgesics. Such treatments, however, are of limited value and have shown improvement only in patients with mild to moderate stomatitis.

TRAUMEEL S® is a homeopathic-complex remedy that has been sold over-the-counter in pharmacies in Germany, Austria, and Switzerland for over 50 years. It contains extracts from the following plants and minerals, all of them highly diluted (10^-10^-9 of the stem solutions): Arnica montana, Calendula officinalis, Achillea millefolium, Matricaria chamomilla, Symphytum officinale, Atropa belladonna, Aconitum napellus, Bellis perennis, Hypericum perforatum, Echinacea angustifolia, Echinacea purpurea, Hamamelis virginica, Mercurius solubilis, and Hepar sulfuris. Information from the manufacturer indicates that TRAUMEEL S® is used normally to treat trauma, inflammation, and degenerative processes.

Informal experience in patients with chemotherapy-related stomatitis suggests that the condition may respond to treatment with TRAUMEEL S® homeopathic-complex remedy. Based on this and subsequent positive results from a preliminary open study in 20 patients with stomatitis who were treated with TRAUMEEL S® compared with 7 untreated, randomly selected patients, we decided to conduct the randomized, placebo-controlled, double-blind clinical trial reported here.

MATERIALS AND METHODS

Patients
Thirty-two consecutive patients who were admitted to Schneider Children’s Medical Center, ages 3-25 years, suffering from malignant diseases and underwent BMT were enrolled. Patients had undergone allogeneic or autologous stem cell transplantation. The
study was approved by the ethical committee at the Rabin Medical Center, and informed, written consent was obtained from parents and/or guardians of all children prior to their enrolment in the study after a full explanation of the benefits, potential hazards, and procedures involved in the study to the patients and their parents and/or guardians.

**Study Medication**

For this study, both TRAUMEEL S and placebo were provided by the HEEL Company (Baden-Baden, Germany) in sterile, 2.2 mL ampoules. Solutions of TRAUMEEL S were prepared by diluting the active substance in saline, according to the German Homeopathic Pharmacopoeia (HAB). The placebo consisted only of saline. The active medication and placebo did not differ in color, taste, or odor.

TRAUMEEL S is manufactured according to the European Union Guidelines on Good Manufacturing Practice for Medicinal Products and in accordance with the HAB. The physical and microbiologic controls of the medications were according to the European Pharmacopoeia specifications.

Extensive safety data from a large survey of TRAUMEEL S showed adverse events in only 0.0035% of patients, despite its use in over 3.5 million patients (manufacturer’s own survey). Adverse effects reported were mostly skin reactions to the cream or local pruritus as a reaction to injection. However, because TRAUMEEL S contains dilutions of substances that may be regarded as toxic, we calculated the content of one of the most toxic substances, a mercury salt, in the medication. Assuming that a patient will have to be treated with TRAUMEEL S for 1 week, he or she will receive 35 ampoules. The mercury concentration of one ampoule is 0.5 ng/mL, giving a total amount of ingested mercury of approximately 17.5 ng per week. This compares favorably with the permitted mercury content of drinking water according to German law (0.001 mg/L). Thus, a 1-week treatment of TRAUMEEL S contains approximately 10^4 of the amount of mercury deemed permissible in 1 L of drinking water.

**Study Procedures**

Thirty-two patients received various conditioning regimens for 5-8 days followed by autologous (16 patients) or allogeneic (16 patients) stem cell infusion on Day 0. Patients were randomized to receive either placebo or TRAUMEEL S on Day 2 of the study in addition to twice-daily mouth washes with chlorhexidine, oral amphoterin B, and gentle tooth brushing (institutional standard for mouth care).

Packages of TRAUMEEL S and placebo were prepared by the Heel Company and were identified by serial number only. The code showing the treatment corresponding to each serial number was kept by the company, the study coordinator (M.O.), and the statistician (L.S.F.). The code was not broken until the completion of the trial. Treatment was started on Day 2 after stem cell transplantation, so that treatment began before the first symptoms of stomatitis (e.g., dryness and/or soreness of the mouth) were observed. The peak incidence of mucositis is typically 5-7 days after transplantation. Fifteen evaluable patients received placebo, and 15 evaluable patients received TRAUMEEL S. Patients were instructed to rinse their mouths vigorously with the solution for a minimum of 30 seconds before swallowing. In addition, patients were directed to keep the liquid as long as possible on particularly troublesome lesions in their mouth. This procedure was repeated five times daily.

The World Health Organization (WHO) grading system for mucositis (Table 1) was used to evaluate stomatitis in each patient. In addition, a subjective scoring system was used in which either the patient or the parents were asked to judge the degree of oral pain and discomfort, dryness of mouth and tongue, dysphagia, and ability to swallow. A five-grade system was used (Grade 0, no complaints; Grade 1, very severe complaints, unable even to swallow liquids). The time to worsening of stomatitis was evaluated as the time from randomization to the day when the mucositis score increased from that recorded at baseline. Patients were evaluated at least once every 2 days. All evaluations were performed blind by the same observer (the study nurse). The trial continued until the patient symptomology had been scored as Grade 0 on 2 consecutive days or until a minimum of 14 days after the start of TRAUMEEL S or placebo treatment in patients in whom no symptoms developed.

The trial was carried out at the Bone Marrow Transplantation Unit, The Schneider Children’s Medical Center of Israel, Rabin Medical Center, Petach Tikva, Israel. All study forms were collected, stored and transferred to computer for analysis by the study coordinator (M.O.). Statistical analysis was performed at the Department of Mathematics, Statistics, and Computer Sciences, Bar-Ilan University, Ramat-Gan Israel (L.S.F.). The randomization code was prepared by the manufacturer (HEEL Company) and was revealed only on completion of the study. Neither the manufacturer, the study coordinator, nor the statistician was involved in any aspect of the treatment of participating patients.

![Table 1: World Health Organization Grading System for Mucositis](image)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No change</td>
</tr>
<tr>
<td>1</td>
<td>Soreness/erythema (painless)</td>
</tr>
<tr>
<td>2</td>
<td>Erythema (painful), ulcers; can eat solids</td>
</tr>
<tr>
<td>3</td>
<td>Ulcers; requires liquid diet only</td>
</tr>
<tr>
<td>4</td>
<td>Alimentation not possible</td>
</tr>
</tbody>
</table>

**Statistical Analysis**

All statistical analyses were done on an intent-to-treat basis unless indicated otherwise. That is, each patient was considered to be allocated randomly to a group regardless of the treatment actually received. The two main treatment comparisons, as specified in the protocol, were of the area under the curve (AUC) for stomatitis symptoms, and the time to first worsening of stomatitis symptoms. Both are based on the WHO grading system.

The AUC is equivalent to the sum of the grade on each day from the start of TRAUMEEL S or placebo treatment. It therefore incorporates both severity and duration of symptoms. When grades were recorded every other day, we used linear interpolation to estimate the stomatitis score on those days when evaluation did not occur. Because the AUC score distribution was not normal, statistical comparison was performed using the two-sample Wilcoxon rank-sum test.

Most patients (77%) started TRAUMEEL S or placebo treatment before the onset of symptoms. In these patients, therefore, the time to worsening of symptoms was the same as the time to the start of symptoms. Consequently, the time to worsening differed from time to first development of symptoms in only 25% of patients (17% with Grade 1 symptoms and 6% with Grade 2 symptoms). The statistical comparison of this endpoint was performed using the log-rank test. All P values reported are two-sided.
RESULTS

Patients

A total of 32 patients were enrolled in this trial. However, two patients (one in the TRAUMEEL S treatment group and the other in the placebo group) received a single dose of study drug but then refused further treatment, complaining of nausea. These patients were not evaluated subsequently for stomatitis and, thus, cannot be included in this analysis. Fifteen patients each remained in the TRAUMEEL S group and the placebo group. The distribution of patient characteristics for each group is shown in Table 2. The groups were comparable with regards to age, gender, type of BMT, granulocyte-colony stimulating factor treatment and prophylaxis against graft versus host disease (GVHD). However, there were some differences in the distribution of diseases between the groups. There were seven patients versus three patients with acute myelogenous leukemia (AML) and zero patients versus three patients with lymphoma in the TRAUMEEL S and placebo groups, respectively. In addition, the three patients who underwent a higher risk BMT (haploidentical or cord blood) all were allocated randomly to the TRAUMEEL S treatment group. The use of concomitant medication, including analgesic treatment, was comparable in both treatment groups.

There was doubt regarding the stomatitis score of Patient 12 as a result of an administrative error. Our policy in areas of doubt was to take the value less favorable to the TRAUMEEL S treatment group. In this instance, the choice was between an AUC score of either 38 or 0, and we used the score of 38. In addition, one patient who was allocated to the placebo group inadvertently received TRAUMEEL S. However, this patient was still considered part of the placebo treatment group, and it is interesting to note that this patient had the second lowest stomatitis AUC score in the placebo treatment group. This patient was included in the analysis according to the intent-to-treat principle and to guard against any bias in the study. Exclusion of this patient from the analysis would have increased the difference between the treatment groups (in favor of TRAUMEEL S). In view of the double-blind design and the intention-to-treat analysis used, it seems unlikely that these irregularities would have substantially affected the results of the study.

Efficacy

The stomatitis AUC scores, together with the times to first worsening, are summarized in Table 3. Stomatitis AUC scores range from 0 to 56. Five patients (33%) allocated to the TRAUMEEL S group did not develop stomatitis (AUC score, 0) compared with 1 patient (7%) from the placebo group. The mean AUC scores were 10.4 in the TRAUMEEL S group and 24.3 in the placebo group. This difference was statistically significant (Wilcoxon rank-sum score, 167.5; expected score, 232.5; \( P < 0.01 \)) and suggests that TRAUMEEL S treatment reduced the severity and/or duration of stomatitis compared with placebo.

In the group of 22 patients age <15 years, the mean AUC score for stomatitis was 11.0 in the TRAUMEEL S group and 25.9 in the placebo group. The Wilcoxon rank-sum test for the difference remained statistically significant (Wilcoxon rank-sum score, 93.0; expected score, 126.5; \( P < 0.01 \)). Thus, the difference remains only if younger patients are considered.

Seven patients (47%) in the TRAUMEEL S treatment group and 14 patients (93%) in the placebo group experienced worsening of symptoms during treatment. The log-rank test indicated that there was a statically significant difference (chi-square test, 13.4 with 1 degree of freedom, \( P < 0.001 \)) between the two groups in the time to worsening of symptoms. In those patients whose symptoms worsened, the median time to worsening was 4.7 days in the TRAUMEEL S group and 4.0 days in the placebo group. These results indicate that symptoms were much less likely to worsen in patients receiving the TRAUMEEL S treatment than in those receiving the placebo, but that, among those whose symptoms did worsen, there was little difference in the median time to worsening of stomatitis between the two treatment groups.

Subjective Symptom Score

The maximum symptom scores for dryness of mouth, oral pain, and eating difficulty over the first 7 days of TRAUMEEL S and placebo treatment are shown in Figure 1. These data were recorded at regular intervals over the 7-day treatment period. These results are very similar to the stomatitis AUC score results: Patients in the TRAUMEEL S group showed a clear reduction in severity of symptoms in all three categories, as indicated by changes in the symptom grading system, compared with the placebo group.

Table 2: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Traumeel S</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (no.)</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>Mean (SD)</td>
<td>10.1 (7.0)</td>
</tr>
<tr>
<td>Distribution</td>
<td>3-4</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>5-9</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>10-14</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>15-19</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>20-25</td>
<td>1</td>
</tr>
<tr>
<td>Gender (no. of males) (%)</td>
<td>8 (53)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Diagnosis (%)</td>
<td>AML 3 (20)</td>
<td>7 (47)</td>
</tr>
<tr>
<td></td>
<td>ALL 1 (7)</td>
<td>2 (13)</td>
</tr>
<tr>
<td></td>
<td>CML 1 (7)</td>
<td>1 (7)</td>
</tr>
<tr>
<td></td>
<td>Lymphoma 3 (20)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other a</td>
<td>7 (47)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>BMT (%)</td>
<td>Allogeneic 8 (53)</td>
<td>7 (47)</td>
</tr>
<tr>
<td></td>
<td>Autologous 7 (47)</td>
<td>8 (53)</td>
</tr>
<tr>
<td>GCSF</td>
<td>4 (27)</td>
<td>4 (27)</td>
</tr>
<tr>
<td>GVHD prophylaxis (%)</td>
<td>CSA only 1 (7)</td>
<td>2 (13)</td>
</tr>
<tr>
<td></td>
<td>CSA + methotrexate 3 (20)</td>
<td>4 (27)</td>
</tr>
<tr>
<td></td>
<td>CSA + steroids 3 (20)</td>
<td>1 (7)</td>
</tr>
<tr>
<td></td>
<td>None 8 (53)</td>
<td>8 (53)</td>
</tr>
</tbody>
</table>

AML: acute myelogenous leukemia; ALL: acute lymphoblastic leukemia; CML: chronic myelogenous leukemia; BMT: bone marrow transplantation; GCSF: granulocyte-colony stimulating factor; GVHD: graft versus host disease; CSA cyclosporine A; SD: standard deviation.

a Other diagnoses in the TRAUMEEL S group: one neuroblastoma, one aplastic anemia, one thalassemia, one Ewing sarcoma, and one medulloblastoma.

Other diagnoses in the placebo group: one neuroblastoma, one Wilms tumor, two aplastic anemia, one thalassemia, one Ewing sarcoma, and one Fanconi syndrome.
Safety and Tolerability

There was a high incidence of serious complications but with no significant difference between the groups, as expected in a group of patients undergoing BMT. GVHD occurred in three patients in the TRAUMEEL S group compared with six patients in the placebo group, sepsis occurred in three patients in the TRAUMEEL S group compared with eight patients in the placebo group, and gastrointestinal complications occurred in no patients in the TRAUMEEL S group compared with five patients in the placebo group. Four patients with venous-occlusive disease occurred in the TRAUMEEL S group compared with none in the placebo group, and pneumonitis occurred in four patients in the TRAUMEEL S group compared with none in the placebo group. Some patients developed more than one of these complications. There was no difference in the incidence or duration of severe neutropenia between the two treatment groups.

There was no significant difference in the number of deaths between the TRAUMEEL S and placebo groups in a follow-up of 44 weeks. Only one death occurred during the study period (to Day 20).

DISCUSSION

Currently available treatments for chemotherapy-induced stomatitis are of limited efficacy in preventing or ameliorating it. The effect of local treatment is short lived, and the medications often have an unpleasant taste. Moreover, the risk of absorption limits the frequency with which some of these drugs may be used in small children and in elderly. For these reasons, the potential benefits of treatment with TRAUMEEL S are of particular interest.

This study demonstrated a statistically significant and clinically relevant difference in efficacy between TRAUMEEL S and placebo in the treatment of stomatitis in children undergoing stem cell transplantation. The strategy of analysis employed in this trial protects against any bias toward TRAUMEEL S. For example, a patient who developed stomatitis on the day that TRAUMEEL S was discontinued (Day 20) was classed as having stomatitis despite developing the condition after treatment was stopped. Patient 10, who accidentally received TRAUMEEL S instead of placebo, still was considered of the placebo group and, in fact, had the second lowest stomatitis AUC score in this group. In addition, there was an excess of patients with lymphoma and a deficit of those with AML in the TRAUMEEL S group. Because it was observed that AML patients had, on average, slightly lower AUC scores compared with other patients in this trial (data not shown), any resulting bias would not benefit the TRAUMEEL S group. Finally, the

Table 3: Stomatitis Area Under the Curve Scores and Time to First Worsening of Symptoms by Allocated Treatment

<table>
<thead>
<tr>
<th>Patient</th>
<th>AUC (days)</th>
<th>Time to worsening (days)</th>
<th>Patient</th>
<th>AUC (days)</th>
<th>Time to worsening (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>&gt; 8</td>
<td>2</td>
<td>27.5</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>&gt; 18</td>
<td>4</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>&gt; 9</td>
<td>5</td>
<td>16</td>
<td>2-3</td>
</tr>
<tr>
<td>7</td>
<td>20</td>
<td>4-5</td>
<td>8</td>
<td>36</td>
<td>1-2</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>3-5</td>
<td>10</td>
<td>4</td>
<td>6-7</td>
</tr>
<tr>
<td>12</td>
<td>30</td>
<td>20</td>
<td>11</td>
<td>56</td>
<td>4</td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td>&gt; 13</td>
<td>14</td>
<td>14</td>
<td>2-3</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>&gt; 13</td>
<td>16</td>
<td>20</td>
<td>2-3</td>
</tr>
<tr>
<td>17</td>
<td>0</td>
<td>&gt; 5</td>
<td>18</td>
<td>31</td>
<td>10-11</td>
</tr>
<tr>
<td>19</td>
<td>17</td>
<td>5</td>
<td>20</td>
<td>21</td>
<td>3</td>
</tr>
<tr>
<td>22</td>
<td>0</td>
<td>&gt; 10</td>
<td>21</td>
<td>0</td>
<td>&gt; 6</td>
</tr>
<tr>
<td>23</td>
<td>17</td>
<td>4-7</td>
<td>24</td>
<td>26.5</td>
<td>5</td>
</tr>
<tr>
<td>25</td>
<td>3</td>
<td>&gt; 8</td>
<td>26</td>
<td>45</td>
<td>4</td>
</tr>
<tr>
<td>28</td>
<td>5</td>
<td>7</td>
<td>27</td>
<td>35</td>
<td>10</td>
</tr>
<tr>
<td>30</td>
<td>26.5</td>
<td>2-3</td>
<td>29</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>Mean</td>
<td>10.4</td>
<td>6.9</td>
<td>Mean</td>
<td>24.3</td>
<td>4.3</td>
</tr>
<tr>
<td>Median</td>
<td>5.0</td>
<td>4.7</td>
<td>Median</td>
<td>21.0</td>
<td>4.0</td>
</tr>
</tbody>
</table>

AUC: area under the curve

a) Test for difference in AUC: Wilcoxon rank sum score, 167.5; expected score, 232.5 (P < 0.01).
b) Test for difference in time to worsening: chi-square test, 13.4 with 1 degree of freedom (P < 0.001).
c) The patient received TRAUMEEL S® accidentally.
d) There was doubt regarding the AUC score and time to worsening. An alternative interpretation would be AUC, 0; time > 19 days.
e) Means and medians of uncensored times only are shown.
three transplant patients who were at the highest risk were allocated randomly to the TRAUMEEL S group. These patients subsequently died, two of them within 3 months of BMT. This may account for the somewhat higher number of deaths among patients in the TRAUMEEL S group. Because the AUC scores for these three patients were 0, 17, and 38, there is no evidence that these higher risk transplantation patients had less severe stomatitis.

Initial observations of treatment with TRAUMEEL S suggest that it is almost free from adverse effects. In addition to the patients in this trial, TRAUMEEL S has been given to over 80 patients receiving chemotherapy on an outpatient basis at the Schneider Children’s Medical Center. With the exception of one patient in the trial who stopped treatment on the first day and two other children who complained of nausea, no other acute adverse effects have been reported.

The mechanism of action of TRAUMEEL S remains unknown. It also is unclear whether only one of its components is biologically active or whether the effects are due to the action of several components. The marked effects seen in this study were achieved using a solution of TRAUMEEL S containing ingredients in very low concentrations. Some of the ingredients of TRAUMEEL S are regarded by homeopaths as remedies with anti-inflammatory properties (Belladonna, Aconitum, Mercurius, Hepar, and Chamomilla) or mucoprotective properties (Calendula and Hamamelis). Arnica is one of the main remedies used in homeopathic treatment of trauma. Arnica, Calendula, Hamamelis, and Millefolium are believed to have antimigratory properties. Echinacea purpurea are thought to be immunostimulatory. Hypericum has been used in patients with neural injury. This suggests that several components may play a role in the mechanism of action of TRAUMEEL S. Indeed, the observation that such a strong response is associated with such small quantities of the different remedies in TRAUMEEL S suggests that a synergistic effect may be involved. However, further research is needed to identify which component(s) are the active compound(s).

The effect of orally administered TRAUMEEL S seems to be isolated to the oral mucosa. Patients with mucositis of other areas of the alimentary tract, for example, esophagitis, enteritis, or proctitis as assessed by subjective complaint (diarrhea and rectal or esophageal pain), did not respond to the TRAUMEEL S administered orally in our trial. Furthermore, there was no difference between the two groups in the median number of days with severe neutropenia. This supports the hypothesis that the effect of this homoeopathic drug is a local one.

The localized effect of TRAUMEEL S also is important for another reason, which has relevance to the general problem of complementary medicine in the treatment of patients with malignant disease. If complementary medical treatment in reality has no biologic effect, then at least it will do no harm. However, if it does have a biological effect, and given our lack of understanding of the mechanisms of action of TRAUMEEL S and homeopathic medicine in general, concerns may be raised about deleterious systemic effects, for example, increasing the resistance of the malignant cells to chemotherapy. Because the effect of TRAUMEEL S appears to be only local, this concern becomes less relevant.

In conclusion, this double-blind, controlled study showed that TRAUMEEL S significantly reduces the severity and duration of chemotherapy-induced stomatitis in children undergoing BMT. TRAUMEEL S appears capable, at least in part, of ameliorating a problem that not only causes considerable suffering to patients, but often limits the possibilities of aggressive treatment with chemotherapy. Because there are few effective, conventional treatments for patients with chemotherapy-induced stomatitis currently available, the significance of treatment with TRAUMEEL S becomes apparent. An effective treatment for stomatitis would allow more aggressive chemotherapy treatments, particularly in children, and, consequently, would be likely to improve the success rates of many chemotherapy protocols. Our study population is small and includes patients with a variety of diagnoses who received several different forms of conditioning regimens. Confirmation of our results in a larger trial in patients receiving BMT or other intensive chemotherapy protocols is needed. Therefore, we are planning to extend our investigations to a large-scale, multicenter study to evaluate the efficacy and safety of TRAUMEEL S in the treatment of adults who are at risk for chemotherapy-induced stomatitis.

REFERENCES

Case Study

Presentation:
14 year old male, asthma, otitis media, sinusitis, eczema, headaches

History of patient:
- At birth diagnosed with IgA subclass 2 and 4 deficiencies
- Onset of otitis media (OM) at 2 months of age, occurring at least once a month
- Tympanostomy, removal of tonsils and adenoids, sinus flush at 2 years of age (YOA)
- Occasions of very high fevers as an infant with colds
- Bacterial pneumonia at 2 YOA prior to onset of asthma
- Onset of asthma at 2 YOA, eczema onset at 8 YOA (scalp, chest, groin)
- Asthma triggers include viral infections, exercise, cold weather, and allergies
- Symptoms with asthma include croupy cough with barking and/or hacking which is paroxysmal in nature, shortness of breath, no wheezing
- Attacks were occurring every one to 2 months
- In the past, he was treated with Singulair® (montelukast sodium) once daily since 5 years, Ventolin® (salbutamol) 3 puffs t.i.d. since 2 YOA, Atrovent® (ipratropium bromide) 2 puffs b.i.d. since 8 years, and Qvar® (beclamethasone dipropionate) 2 puffs daily since 2 years
- Even on these medications, with various changes and adjustments, he has never been stable with respect to the asthma, peak flows never > 300 L/min
- Naturopathic treatment started in June 2004

Treatment Plan:

06/30/04
- Pulsatilla compositum: 1 ampoule 3 times weekly, per os
- Tartephedreel: 10 drops t.i.d.

07/21/04
- Tartephedreel: 10 drops t.i.d.
- Pulsatilla compositum, Engystol, Zeel comp., Ubicoenzyme: by inhalation, 1 ampoule of each 3 times weekly
- Pyridoxal-5-Phosphate 50 mg daily
- Beta carotene 7500 UI, ascorbic acid 500 mg, vitamin E 150 IU, selenium (citrate) 50 micrograms (ACE+ Se by Thorne Research®) 1 capsule b.i.d.
- DHA 200 mg, EPA 900 mg, other omega-3 oils 100 mg, vitamin E 22 IU (ProEPA® by Nordic Naturals®) 1 capsule daily

08/11/04
- Not needing any inhalers at all
- No cough, no shortness of breath
- When walking dog, no coughing at all
- Peak flows average 370 L/min, 1 week ago was 450 L/min

09/08/04
- With physical education class at school, remaining asymptomatic with exertion, taking Ventolin® 15 minutes prior to class with no difference
- Treatment change:
  - Pulsatilla compositum, Tuberculium-Injeel forte, Funiculus umbilicalis suis-Injeel: by inhalation, 1 ampoule of each 2 times weekly
  - Continue Tartephedreel and other supplements

10/27/04
- Peak flows generally around 400+ L/min now
- Not using any puffers at all
- Treatment:
  - Finish and stop inhalations for now
  - Continue with supplements

11/09/04
- All medications finished, starting to feel worse again
- Peak flows now decreased to below 300 L/min
- Treatment:
  - Restart inhalation with Pulsatilla compositum, Engystol, Zeel comp., and Ubicoenzyme, 1 ampoule of each 3 times weekly, along with Tartephedreel, 10 drops t.i.d., continue other supplements

11/17/04
- Improvement within several days of restarting inhalation treatments
- Peak flows back to 370-400 L/min
- Treatment:
  - Continue inhalation until the end of December 2004, along with supplements

12/21/04
- Peak flows 380-400 L/min on average, with very occasional drops
- Not using puffers at all
- Sinuses bothering lately, eczema on scalp becoming worse lately
- Treatment:
  - Continue as per 11/09/04 with inhalation, Tartephedreel, and supplements
  - Add Euphorbium compositum nasal spray, bilaterally 1-2 sprays b.i.d.

02/10/05
- Peak flows now maintained between 400-450 L/min daily
- One incidence of a decline (to 350 L/min) with a cold for 4 days, but no significant change in symptoms
- Tartephedreel and inhalation therapy ceased
- Euphorbium compositum nasal spray PRN
- Supplements decreased: Pyridoxal-5-Phosphate 50 mg daily, ACE+Se 1 capsule daily, ProEPA 1 capsule daily

Conclusion
Patient and parents are very satisfied with the outcome of treatment. He has not suffered from any asthma attacks since initiation of treatment. Incidentally, the eczema has also improved. Headaches and sinusitis have been resolved. There has been no other incidence of otitis media since the beginning of treatment.
Post-surgical follow-up treatment in canine mammary tumors with biological remedies


Original article in German*

Introduction
Tumor diseases currently represent the main cause of death in dogs and cats (Withrow and Machwen, 1996). Among tumor diseases in dogs, mammary tumors in turn are one of the most frequently diagnosed neoplastic changes, making up a proportion of about 40-50% in bitches (Simon et al. 1996), and in rare cases (1.3%) mammary tumors can also occur in male dogs (Simon et al. 1996).

Surgical removal of tumors is still to be regarded as the treatment of choice. Needless to say, the unsatisfactorily high incidence of recurrences and metastases and the closely correlated survival rate cannot be improved significantly by removal of the tumor. In addition, in recent years it has also been shown that the proportion of malignant tumors among mammary tumors in bitches, which was previously held to be not too high, is indeed in the region of 50% or more, up to 70 or 80%. Since Homotoxicology, in the context of its pathology offers a theory of tumor formation and also provides appropriate remedies to eliminate causal factors, it was obvious to investigate the effectiveness of this anti-homotoxic treatment on tumor diseases.

Treatment with intermediate catalysts
Tumor diseases in particular are characterized by impaired cell respiration, leading to cell damage and therefore, disease. By administration of certain preparations with homeopathic constituents, so-called intermediate catalysts, the organism is helped to compensate for intermediate dysfunctions in the citric acid cycle and in the respiratory chain.

The preparation Coenzyme compositum (manufacturer: Biologische Heilmittel Heel GmbH, Baden-Baden) contains salts and acids of the citric acid cycle as intermediate catalysts in homeopathic form. It is used generally for chronic or degenerative diseases and for disturbances in enzymatic functions.

Ubichinon compositum (Heel, Baden-Baden) is also indicated for severe states of disease, such as degeneration or degradation of tissues where the endogenous defense and repair mechanisms are no longer adequate. The constituent ubiquinone contains reactive carbonyl groups. Ubiquinone has a potent regenerative effect on blocked enzymes, especially in the respiratory chain. The medicinal action of quinone compounds was worked out theoretically and experimentally by the American clinician Koch (1981). The preparation Para-Benzochinon-Injeel forte (Heel, Baden-Baden) also has a regenerating effect on cell respiration.

As well as these cell metabolism-activating substances, biotherapeutics which lead out toxins are additionally used in treating tumor diseases. Lymphomyosot (Heel, Baden-Baden) is a suitable combination preparation for this. In this study, Lymphomyosot was used orally as drops along with an injection treatment. All the preparations mentioned are homeopathic remedies.

Study type, material and method
The investigation was designed as a prospective, open clinical study and the results were then compared with an external control. Between May 1996 and December 1998, 34 bitches brought into the Small Animal Clinic of the Veterinary Institute of the Georg-August University in Göttingen, Germany with proliferations in the teats were given postoperative biological treatment. The age of the dogs was between 6 and 17 years (average age 11.1 years).

Treatment concept, investigation and control plan
A standardized treatment plan, which in a similar form has already been described as effective when used in practice (Boynes 1992, Braun 1986, Gratz 1981), was specified for the study (Table 1). The treatment aim was to prolong survival times and reduce the incidence of recurrences or metastases.

<table>
<thead>
<tr>
<th>Table 1. Treatment scheme combined to surgical removal of mammary tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coenzyme compositum + Ubichinon compositum</strong></td>
</tr>
<tr>
<td><strong>Para-Benzochinon-Injeel forte</strong></td>
</tr>
<tr>
<td><strong>Lymphomyosot drops</strong></td>
</tr>
</tbody>
</table>

The biological treatment was started one day postoperatively with a mixed injection of Ubichinon compositum and Coenzyme compositum. The second injection of Ubichinon compositum, Coenzyme compositum and Para-Benzochinon Injeel forte was given in the context of wound control (3rd or 4th day postoperative). The treatment was continued according to this plan twice weekly. After the operation, the patients’ owners were also given Lymphomyosot drops, which were administered in parallel once daily in the stated dosage via food.

The treatment series were carried out over 4 weeks, then after a 4-6 week pause, another 4 weeks of treatment.
The treatment described was carried out for four weeks. This was followed by a pause of 4-6 weeks. The patients then again received Lymphomyosot drops orally for four weeks, and a mixed injection, only once a week, of Ubichinon compositum and Coenzyme compositum with Para-Benzochinon-Injeel forte. After the second treatment period, no further treatment took place in this study.

**Results and discussion**

Of the 31 samples investigated, 26 (83.9%) were classified as malignant and 5 (16.1%) as benign or not neoplastic. The adenocarcinomas showed the highest proportion here at more than 50%, followed by the malignant mixed tumors with 16.1%. Since the treatment had already been started before the histology results were available, the treatment was also continued on the benign or non-neoplastic teat proliferations (n=3) and included in this documentation. Since the age and breed distribution compares very well with other studies, a study by the Veterinary College in Hannover (Simon et al. 1996) was used as a so-called external control.

**Survival rate and incidence of metastasis**

The percentage data given in the following, just as in the literature works cited, relate to the total population of the study unless stated otherwise.

With the biological after-treatment, a survival rate after one year of 73.5% was achieved (26.5% died). In the study of Simon et al. (1996), in contrast, 37.3% did not survive the postoperative investigation period of one year. The mortality rate after two years in the Bostock (1975) study is 48%. With biological after-treatment, in this study, a proportion of dead animals of 35.3% resulted. The 2-year survival rate also is therefore over 10% more favorable than without after-treatment.

Also in respect of recurrences, the results with biological after-treatment are more favorable than in the case of animals from other studies treated purely by surgery. 49.3% of the bitches operated on (based on the total population) showed recurrences and/or metastases within one year in the study of Simon et al. (1966). By comparison, in this study, the recurrence or metastasising frequency after one year was 23.5%. Therefore, this results in a very clear advantage for biological after-treatment, since the incidence of recurrences or metastases was more than 25% below the values quoted in the literature. If only the patients with malignant tumors are considered, with after-treatment there is a rate of recurrence or metastasising after one year of 26.9%, while the corresponding value of Simon et al. (1966) is 45% (mammary 30%, lung 15%). From this point of view, a treatment advantage of approximately 20% is thus possible.

With the possibility of using the same biological treatment plan preoperatively to achieve a better precise demarcation of tumors with highly infiltrative growth, the prerequisites for complete removal of tumors can also be improved. Even with purely conservative treatment, which in some cases represents the only measure which can be carried out, a positive effect is generally found (halt of growth or reduction in size, sometime better demarcation; Kurth 2000).

**Acceptance and tolerability**

No intolerance symptoms were observed in the study either by the veterinarians or by the animal owners. A remarkable advantage of the treatment used here compared with the therapeutic alternatives, such as, for example, chemotherapy, is therefore to be seen as very good tolerability. All animal owners with whom the possibility of biological after-treatment was discussed were prepared to carry out this treatment. The acceptance overall is therefore higher than with chemotherapy, which was categorically rejected by 27% of those asked by Simon et al. (1996). No particular safety precautions are required when handling the preparations used here.

**Conclusion**

The following conclusions can be drawn from the study:

- The postoperative treatment tested, with 2 treatment series in the first 3 months after the surgery, improved the survival rate after 1 year and after 2 years by at least 10% compared with literature data (average age at operation: 11.1 years).
- The rate of recurrence or metastasis 1 year postoperative was more than 25%, taking into account the total population, or approximately 20% taking into account only the malignant cases, both of which are better than literature data.

In spite of the only limited conclusiveness of purely percentage data and the contributory effect of individual factors (age at the time of the operation, degree of metastasising at the first appointment, distribution of the types of tumors and malignancy levels), a clear trend is detectable: biological treatment according to the plan described above has a positive influence on the phase after removal of the tumor. Good results were achieved above all on mammary tumors of low or moderate malignancy. The frequency of recurrence and metastasising and the associated survival time were improved significantly compared with literature data.

The following can therefore be recommended to optimize the treatment: the restriction to two treatment series imposed on experimental grounds can usually be lifted for an individual patient in the practice. From empirical observations, about 3 - 4 treatment series a year are recommended. A treatment plan for highly malignant tumors should be developed and tested, and such a study again is currently in progress in Göttingen.

**Literature**


*The original article has been modified and truncated for this publication.*
Looking for a safe & effective alternative to Vioxx® and Celebrex® for your patients?

- As effective as COX II inhibitors (celecoxib and rofecoxib) in treating mild to moderate osteoarthritis of the knee and is significantly better tolerated¹
- As effective as diclofenac² and hyaluronic acid³
- Modulates 5-lipoxygenase and cyclooxygenase⁴
- Is exceptionally well tolerated
- Causes no adverse effects on renal, cardiovascular or nervous systems
- Ideal for long-term treatment and is suitable for patients of all ages
- Can be safely combined with other homeopathic or allopathic medications