The rate of complications that occur at a colostomy site range from 15% to 34%\(^1\) and therefore, the massive presence of bacteria secondary to local exposure to the intestinal content may lead to cellulitis, abscess, ulceration, and fistula.\(^1-4\) Reported rates of septic complications of the pericolostomic region range from 2.2% to 30%.\(^4-9\)

A morpho-functional difference is present between the skin tissue of the abdominal wall and that of the anal region.\(^10\) The skin of the anal canal region has specific traits that allow frequent contact with the enteric bacterial content with little or no clinical effect. Nevertheless, this condition occurring in the abdominal wall in the presence of a colostomy or an entero-cutaneous fistula is still not completely clarified, since there are no studies demonstrating the changes in the local immunological system determined by the

### Understanding the Effects of Colostomy-induced Alterations on Cutaneous Immunity

Valdemir José Alegre Salles, MD, PhD;\(^1\) Sarhan Sydney Saad, MD, PhD;\(^2\) Marcello Fabiano Franco, MD, PhD;\(^2\) Delcio Matos, MD, PhD\(^2\)

**Abstract:** Objective. This study describes the immunological response in the dermal layer of the peri-colostomic region, and identifies and quantifies the cellular elements present. Methods. Forty-one patients with colostomies present for more than 8 weeks were included. Thirty-one patients were men (75.6%) and 10 were women (24.4%) with an average age of 49.9 years. Thirty-four patients (82.9%) were classified as surgical risk class I and 7 patients (17.1%) were classified as class II. The data were analyzed statistically using the Mann-Whitney, Kruskal-Wallis, and Dunn tests using 0.05 or 5%. Results. Analysis of the immuno-cellular response regarding the time of permanence of the colostomy showed a significant frequency of T lymphocytes (pan T-CD3) in all the time periods in a significantly superior number (\(P < 0.001\)) than the B lymphocytes (CD20) and the T lymphocytes-natural killer (CD57). T-helper cells (CD4) were present in larger numbers in the first three periods. Conclusion. The presence of a colostomy for more than 8 weeks promotes the development of a chronic inflammation and an immuno-cellular response in the dermal layer of the pericolostomy region. However, its intensity did not demonstrate a statistically significant difference based on time of colostomy existence. The immuno-cellular response in the peri-colostomic dermal area is composed of a major number of T lymphocytes (pan T-CD3) and T lymphocytes-helper (CD4), and is more numerous between the 16th and 20th weeks, whereas, less cellular activity was noted between the 30th and 50th weeks.
ectopic bacterial colonization.

An initial prospective study was conducted in order to determine the prevalence and type of bacteria in the peristomal skin of patients with a colostomy. It demonstrated that the most frequently cultured bacteria were Escherichia coli (91.2%), followed by Bacteroides spp and Peptococcus spp (38.2%), Klebsiella spp (32.3%), and Bacteroides fragilis (29.4%). When the frequency of cultured bacteria was compared to the duration of the colostomy, E. coli was present during all the study periods, while Peptococcus spp increased over time; Bacteroides fragilis and Klebsiella spp were not found in the period after 20 weeks.

The objective of the present study was to characterize the immunological response in the dermal layer of the pericolostomic region by quantifying the role of T- and B-lymphocytes and macrophages in the pericolostomic immunocompetent tissue. This condition can justify the low infection risk index.

**Methods**

A prospective study was conducted among patients at the Federal University of São Paulo Medical School and the University of Taubaté (São Paulo, Brazil) to determine the effects of colostomy-induced alterations on cutaneous immunity. Forty-one patients with temporary colostomies were included in the study period (October 10, 2000–January 10, 2006). The patients had a temporary colostomy of at least 8 weeks duration located either in the transverse or in the sigmoid colon due to reconstruction of the intestinal transit. The Medical Ethics Committee of the Medical School approved the study. All patients were informed of the procedure, agreed to participate in the study, and gave written consent.

Thirty-one patients (75.6%) were men and 10 (24.4%) were women with average age of 49.9 years. Thirty-four (82.9%) were in surgical risk class I and 7 (17.1%) were in class II, as defined by the American Society of Anesthesiology. Twenty patients with malignant colorectal neoplastic disease (in stages B2 and B1, Astler-Coller classification) and 21 patients with benign colorectal disease were studied. Twenty-one patients with benign colorectal disease were also included in the study.

Exclusion criteria included: 1) pericolostomic skin disease (stenosis, cellulitis, prolapse, dermatitis, sepsis) or if the patient had undergone chemotherapy and/or radiotherapy within the previous 30 days; 2) diabetes mellitus, immunosuppressive, and cachectic disorders; 3) infectious or inflammatory processes in other tissues; 4) those under treatment or who had been treated with antibiotics and anti-inflammatory medications within the previous 30 days.

Based on these criteria, a group of 41 patients was formed. The patients were admitted consecutively to the study group and were later placed in subgroups depending on the duration of the colostomy. Patients were classified into four subgroups based on the duration of the colostomy (ie, 8 to 12 weeks [12 patients]; 12.5 to 16 weeks [12 patients]; 20 to 24 weeks [9 patients]; and 30 to 50 weeks [8 patients]).

Skin tissue samples were obtained from the anterior abdominal wall in a site about 30 cm from the colostomy, distant from skin folds and from the inferior margin of the colostomy at roughly 0.5 cm from the entero-cutaneous transition. The colon was prepared following the pre-surgical procedure. No oral antibiotic preparation was used. Antiseptic measures were performed in the dermal pericolostomic region. The results of the immunohistochemical study were expressed as the sum of the number of reactive cells counted in five high-powered fields in the areas of greater concentration of the inflammatory infiltrate.

The histopathologic data were analyzed statistically using Mann-Whitney, Kruskal-Wallis, and Dunn tests. The BioStat software for Windows was utilized for analysis of data and 0.5 or 5% (α ≤ 0.05) was set for rejection of the null hypothesis.

**Results**

To analyze the immunocellular response in the dermal pericolostomic region, the values of T lymphocytes (CD3 positive cells), T helper cells (CD4 positive cells), T cytotoxic cells (CD8 positive cells), B lymphocytes (CD20 positive cells), natural killer cells (CD57 positive cells), and macrophages (CD68 positive cells) were quantified according to the duration of the colostomy. Two independent, blinded pathologists analyzed the samples; the main author assessed their results.

A greater frequency of T lymphocytes was observed in all periods. In the first period, the presence of these cells was 40.4% (1555/3842), in the second 32% (2106/6584), in the third 35% (981/2797), and in the fourth period 34% (525/1547). T helper cells (CD4) were present in larger numbers in the first three periods. In the first period, it was noted in 20.4% (783/3842), in the second in 21.8% (1436/6584) in the third in 21.1% (590/2797), and in the fourth period in 18.1% (280/1547), behind the macrophages (CD68) with 22.1% (342/1547). All data in

Vol. 21, No. 7 July 2009

Salles et al
the dermal peri-colostomic layer were statistically significant ($P < 0.0001$) compared to cell counts in the normal skin. Among the four groups, comparison of the cell counts in the pericolostomic area did not demonstrate a statistically significant difference ($P > 0.05$). The total T lymphocyte, the helper T lymphocyte, and the macrophage cell counts were significantly superior to that of B lymphocytes and natural killer cells, whereas, in the fourth period, the T lymphocyte and macrophage counts macrophages were significantly superior to those of B lymphocytes and natural killer cells (Table 1).

According to the Dunn test, a statistically significant relationship was noted in the cell markers and the numerical relation of the values. The T lymphocytes (CD3 positive cells) were increasingly present in all the periods studied; the macrophage cell counts were significantly superior to the B lymphocyte and natural killer cell counts in the first and fourth periods (Table 2).

**Discussion**

The rate of infectious complications affecting the pericolostomic region has been reported as low, despite the permanent contact of the local skin tissue with intestinal content.

the dermal peri-colostomic layer were statistically significant ($P < 0.0001$) compared to cell counts in the normal skin. Among the four groups, comparison of the cell counts in the pericolostomic area did not demonstrate a statistically significant difference ($P > 0.05$). The total T lymphocyte, the helper T lymphocyte, and the macrophage cell counts were significantly superior to that of B lymphocytes and natural killer cells, whereas, in the fourth period, the T lymphocyte and macrophage

the dermal peri-colostomic layer were statistically significant ($P < 0.0001$) compared to cell counts in the normal skin. Among the four groups, comparison of the cell counts in the pericolostomic area did not demonstrate a statistically significant difference ($P > 0.05$). The total T lymphocyte, the helper T lymphocyte, and the macrophage cell counts were significantly superior to that of B lymphocytes and natural killer cells, whereas, in the fourth period, the T lymphocyte and macrophage counts macrophages were significantly superior to those of B lymphocytes and natural killer cells (Table 1).

According to the Dunn test, a statistically significant relationship was noted in the cell markers and the numerical relation of the values. The T lymphocytes (CD3 positive cells) were increasingly present in all the periods studied; the macrophage cell counts were significantly superior to the B lymphocyte and natural killer cell counts in the first and fourth periods (Table 2).

**Discussion**

The rate of infectious complications affecting the pericolostomic region has been reported as low, despite the permanent contact of the local skin tissue with intestinal content.

the dermal peri-colostomic layer were statistically significant ($P < 0.0001$) compared to cell counts in the normal skin. Among the four groups, comparison of the cell counts in the pericolostomic area did not demonstrate a statistically significant difference ($P > 0.05$). The total T lymphocyte, the helper T lymphocyte, and the macrophage cell counts were significantly superior to that of B lymphocytes and natural killer cells, whereas, in the fourth period, the T lymphocyte and macrophage counts macrophages were significantly superior to those of B lymphocytes and natural killer cells (Table 1).

According to the Dunn test, a statistically significant relationship was noted in the cell markers and the numerical relation of the values. The T lymphocytes (CD3 positive cells) were increasingly present in all the periods studied; the macrophage cell counts were significantly superior to the B lymphocyte and natural killer cell counts in the first and fourth periods (Table 2).

**Discussion**

The rate of infectious complications affecting the pericolostomic region has been reported as low, despite the permanent contact of the local skin tissue with intestinal content.

the dermal peri-colostomic layer were statistically significant ($P < 0.0001$) compared to cell counts in the normal skin. Among the four groups, comparison of the cell counts in the pericolostomic area did not demonstrate a statistically significant difference ($P > 0.05$). The total T lymphocyte, the helper T lymphocyte, and the macrophage cell counts were significantly superior to that of B lymphocytes and natural killer cells, whereas, in the fourth period, the T lymphocyte and macrophage counts macrophages were significantly superior to those of B lymphocytes and natural killer cells (Table 1).

According to the Dunn test, a statistically significant relationship was noted in the cell markers and the numerical relation of the values. The T lymphocytes (CD3 positive cells) were increasingly present in all the periods studied; the macrophage cell counts were significantly superior to the B lymphocyte and natural killer cell counts in the first and fourth periods (Table 2).

**Discussion**

The rate of infectious complications affecting the pericolostomic region has been reported as low, despite the permanent contact of the local skin tissue with intestinal content. However, the skin of patients with a stoma is heavily colonized, increasing the risk of infection at the surgical site. The most frequently cultured bacteria in this region are Escherichia coli, Bacteroides fragilis, Bacteroides spp, and Peptococcus spp. These organisms are also the most common bacteria present in fecal cultures and are the main source of bacterial colonization of the pericolostomic dermis. The data of these studies suggest that a sufficient number of enteric bacteria colonize the dermal pericolostomic layer of the abdominal wall,
which causes local infection.\textsuperscript{11} However, human skin contains the necessary cells and protective mechanisms to begin a self defensive immunological response. The local lymphomononuclear cells interact with the antigens and are regulated and modulated by other cells such as keratinocytes, mast cells, eosinophils, and endothelial cells. Additionally, the Langerhans and dermal dendritic cells provide the cutaneous antigens to the T cells, which induce a specific immune response. Overall, the Langerhans cells, keratinocytes, epidermotropic T cells, and the peripheral satellite lymph nodes comprise the immunological unit responsible for protecting human skin against exogenous and endogenous attacks.\textsuperscript{15}

The interaction between the keratinocytes, Langerhans cells, lymphocytes, and specialized endothelial cells represents the Skin Associated Lymphoid Tissues (SALT). There is an intimate relationship between the immune system and the skin, which together form the cutaneous defense mechanism.

The skin is a natural obstacle and a relatively non-vulnerable barrier that prevents the aggression of the majority of pathogens.\textsuperscript{16} The tissue defense released against an infection consists basically of three mechanisms, which frequently operate in chronological sequence. These protector mechanisms consist of a non-induced innate defense, an induced innate defense, and an adaptive immunological response.\textsuperscript{17} The permanent contact of the peri-colostomie region with the colostomy contents associated with local factors such as humidity, pH, and temperature promote bacterial enteric colonization.\textsuperscript{18,19} Nevertheless, no studies exist regarding the presence of inflammatory or immunological defense mechanisms in this region.

Among the important mechanisms in bacteriological control of the skin are pH and humidity. A low pH plays an important role in preventing infection by inhibiting bacterial growth.\textsuperscript{20} In the ostomy region where the pH and humidity are higher, the permeability of the homeostatic barrier and in the integrity of the stratum corneum are altered, favoring bacterial proliferation.\textsuperscript{21} Basically, the skin is composed of two mutually dependent layers: the epidermis and the dermis. Located below the epidermis, the dermis is made up by collagen, mucopolysaccharides, water, nerves, blood vessels, lymphatics, adnexa, and cells, particularly fibroblasts, mast cells, and macrophages.\textsuperscript{22} The integration of these layers forms a protective barrier against infection that prevents microorganisms from penetrating into the subdermal tissue.\textsuperscript{23} After local trauma, a repair and healing process is initiated\textsuperscript{24} involving different operations such as inflammation, cellular proliferation, and synthesis of elements that comprise the extracellular matrix. Hence, a slight majority of macrophages and fibroblasts is present during the healing process with the synthesis of a new extracellular matrix and restoration of the tissue to its normal appearance on day 26.\textsuperscript{25} The initial inflammatory response has an effective role in tissue protection\textsuperscript{26}; after this period, a significant decrease in the number of macrophages and fibroblasts occurs and maturation of the scar becomes almost acellular.\textsuperscript{27} The macrophages participate in the immune system promoting homeostasis, fighting the infectious agents and the tumoral growth, and aiding in the healing process.\textsuperscript{28} The T lymphocyte component of the immunological unit responsible for human skin protection is located mainly in the dermis close to the post-capillary venular regions, and in the basal layer of the epidermis.\textsuperscript{29} Natural killer cells are large granular lymphocytes that constitute a key component of the human innate immune response. In addition to their potent cytolytic activity, natural killer cells elaborate a host of immuno-regulatory cytokines and chemokines that play a crucial role in pathogen clearance.\textsuperscript{30} The natural killer cells can directly lyse infected cells, secrete cytokines, and interact with dendritic cells to drive the adaptive immune response.\textsuperscript{31}

Microorganisms may penetrate the inferior epidermal region and the superficial dermis, breaking the corneal layer, which is the main barrier to the entrance of exogenous substances.\textsuperscript{24} The persistence of the infectious agents initiate an immunological reaction intensifying the injury to the local skin, which involves a non-specific inflammatory process.\textsuperscript{32} This chain of events occurs in the pericostomie region where permanent contact of fecal matter with the skin promotes a persistent state of local inflammation.

The results of this study demonstrate the alterations of the cutaneous immunity to an unusual bacterial load with a satisfactory control of the invaders determined by the presence of an expressive number of defense cells in the dermal pericostomie layer. This can justify the low infection risk index. The present study cannot affirm that a correlation exists between the types of bacteria isolated and the cell counts due to the low number of cases.

**Conclusion**

The presence of a colostomy for more than 8 weeks promotes bacterial colonization, a chronic inflammatory process, and an adaptive immunocellular response in the
dermal layer of the peri-colostomic region. This immunocellular response in the dermal pericolostomic layer based on the time of permanence of the colostomy is composed of a substantial number of T lymphocytes, T helper cells, T cytotoxic cells, and macrophages. This response reduces the risk of local or systemic infection. New studies employing the same methodology, but involving patients with pericolostomic complications or systemic visceral involvement, should be undertaken to expand the understanding of this surgical condition in order to apply it to a wider group of ostomized patients.

References