

The effects of odontogenic infection on the complete blood count in children and adolescents

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Abstract

Hospital charts of children 2-18 years were reviewed retrospectively and categorized by one of the following diagnoses: (1) dental caries, (2) dental caries with periradicular pathoses, (3) facial cellulitis of dental origin, or (4) periorbital cellulitis (nondental etiology). The CBC values for each patient were tabulated in an attempt to establish a characteristic blood response pattern for the various stages of dental infection. Results showed that a measurable blood response is uncommon until the infection progresses to the stage of acute cellulitis. However, at that stage, a characteristic pattern of blood response is seen for such infections.

In the past, the CBC has been chiefly a tool of the physician. Standard normal values for the various CBC components have been available for nearly 40 years, and in the last two decades clinicians have become adept at utilizing CBC results for making diagnostic, prognostic, and therapeutic recommendations.¹⁻⁷ Thus far, use of the CBC by dentists has been limited; most CBC examinations are ordered as part of a battery of routine laboratory examinations upon admission to the hospital for operative dentistry and oral surgery. However, some CBC examinations are requested for treatment of patients with facial cellulitis of dental origin to monitor the course of the infection and the efficacy of therapy. The various indices of the CBC long have been known as sensitive indicators of the physiologic and pathologic state of the individual.³ White blood cell count and the differential white blood cell counts have been used for the past 75 years to help evaluate infectious and noninfectious diseases.

Manroe et al. demonstrated that a carefully done differential white blood cell count may be of significant help in distinguishing early-onset streptococcal disease from other causes of respiratory distress in neonates.⁴ Zipursky et al. concluded that an elevation of the band neutrophil count above the normal range is a valuable prognostic sign in premature infants in

whom sepsis is suspected. The latter study also demonstrated that an elevation of the neutrophil count without a concurrent increase in the band neutrophil count may occur in patients in whom there is no evidence of infection.⁵ Weitzman, in a review of the medical literature concerning the diagnostic utility of the WBC count and differential count, cites many generally known and accepted conclusions dealing with the effects of infectious and noninfectious entities on the WBC count and the differential count.⁶

The WBC count and differential count are not the only components of the CBC to be affected by infectious processes. Anemia is a common feature of chronic infections and occasionally may complicate acute infection; this usually indicates a hemolytic infection. Clostridial bacteremia may produce massive intravascular destruction of erythrocytes by producing a lecithinase and hemolysins which act on the membranes of red cells and cause their destruction. Anemia is common in cases of subacute bacterial endocarditis, tuberculosis, brucellosis, and chronic pulmonary infections such as lung abscesses and empyema. The anemia of chronic infections usually is normocytic and normochromic but may be normocytic and hypochromic. The platelet count is a valuable test in that isolated thrombocytopenia may develop during the course of some acute gram-positive and gram-negative bacterial infections.⁷

As of this writing, no scientific studies examining the hematologic effects of odontogenic infection as manifested in the routine CBC could be found in the medical or dental literature. It is the purpose of this study to examine the effects of odontogenic infection upon various CBC parameters, and to define a characteristic hematologic pattern for such infections.

Methods and Materials

Hospital charts of patients 2-18 years were reviewed and selected in the following manner. A retrospective search was conducted screening for one of

TABLE 1. Cumulative Summary of Mean and Standard Deviation Values for CBC and Body Temperature Data

	Control Range	Group 1a	Group 1b	Group 2	Group 3
RBC/mm ³	4.32 - 5.12	\bar{x} 4.83 \bar{s} 0.51	\bar{x} 4.60 \bar{s} 0.40	\bar{x} 4.72 \bar{s} 0.55	\bar{x} 4.58 \bar{s} 0.37
Hct %	34.5 - 40.9	\bar{x} 38.4 \bar{s} 3.5	\bar{x} 38.0 \bar{s} 3.2	\bar{x} 37.6 \bar{s} 5.3	\bar{x} 36.77 \bar{s} 3.0
Hgb mg/100 cc	11.7 - 14.1	\bar{x} 12.9 \bar{s} 1.2	\bar{x} 12.84 \bar{s} 1.3	\bar{x} 12.9 \bar{s} 1.3	\bar{x} 12.4 \bar{s} 1.1
MCV u ³	76 - 84	\bar{x} 81.1 \bar{s} 13.4	\bar{x} 82.5 \bar{s} 15.0	\bar{x} 80.9 \bar{s} 4.9	\bar{x} 80.7 \bar{s} 4.6
MCH pg	24.4 - 28.5	\bar{x} 29.3 \bar{s} 5.4	\bar{x} 28.9 \bar{s} 8.5	\bar{x} 27.39 \bar{s} 2.0	\bar{x} 27.6 \bar{s} 4.2
MCHC gm/100 ml	32.1 - 36.1	\bar{x} 33.6 \bar{s} 0.9	\bar{x} 33.8 \bar{s} 0.8	\bar{x} 33.7 \bar{s} 1.47	\bar{x} 33.8 \bar{s} 0.9
Platelets/mm ³	135,000 - 466,480	no data \bar{x} 7,200	no data \bar{x} 7,100	\bar{x} 337,500 \bar{s} 62,077	\bar{x} 394,250 \bar{s} 59,225
Total WBC/mm ³	4,500 - 11,000	\bar{x} 2,200	\bar{x} 2,100	\bar{x} 12,400 \bar{s} 3,600	\bar{x} 15,000 \bar{s} 6,200
Differential WBC	56.0 P 34.0 L 4.0 M 2.7 E .5B 3.0 Bands	no data	no data	73.8 P 18.8 L 5.8 M .9 E .1 B .8 Bands	70.6 P 19.1 L 5.4 M 1.1 E .1 B 3.3 Bands
Body temp. (°F)	98° (acceptable range 97° - 99°)	\bar{x} 98.5 \bar{s} 0.8	\bar{x} 98.6 \bar{s} 0.7	\bar{x} 100.2 \bar{s} 1.40	\bar{x} 100.2 \bar{s} 1.7
Age	\bar{x} 6.9 yrs	\bar{x} 6.4 yrs	\bar{x} 6.1 yrs	\bar{x} 8.4 yrs	\bar{x} 5.9 yrs
Sample size	control population	N = 35	N = 36	N = 40	N = 42

three final diagnoses: (1) dental caries, (2) facial cellulitis secondary to dental origin, and (3) periorbital cellulitis (dental etiology having been ruled out). Group 1 was divided into two subgroups. Group 1a was designated "multiple caries without periradicular pathosis." Group 1b was designated "multiple caries with periradicular pathoses." The subclassification was based upon a thorough review of each patient's dental chart. Multiple caries were confirmed through examination of full mouth radiographs and/or clinical charting. Periradicular pathosis likewise was confirmed through examination of dental radiographs and/or specific mention of single or multiple fistulas or parulis of dental etiology. In Groups 2 and 3, the use of the term "cellulitis" to describe each patient's condition upon admission to the hospital was consistent with the definition given by Schuster and Burnett.⁸ The search was terminated when the number of prospective cases in each of the four groups was 60 (N = 60).

In each group, the patient's medical history was reviewed. Any case with a suspected or positive history of hematologic disease or abnormality was excluded from the study. Also excluded were patients receiving antibiotic therapy and those patients receiving any pharmacologic agent with known hematologic effects.⁹ Final population size for each group

was: Group 1a, N=33; Group 1b, N=36; Group 2, N=40; and Group 3, N=42.

Leukocyte count (WBC count), erythrocyte count (RBC count), hematocrit, hemoglobin concentration, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were analyzed by automated instrumentation in the hospital hematology laboratory. The WBC differential count and the platelet count were completed manually by conventional smear techniques and read by certified technicians.

The CBC utilized for each patient was that obtained upon admission to the hospital. Values for body temperature also were obtained upon admission. All values for body temperature were adjusted to an equivalent oral temperature if taken rectally or in the axillary areas.¹⁰ Control values for each of the component analyses comprising the CBC were standard normal values for the population served by the Cincinnati Childrens's Hospital Medical Center (CHMC). These values were obtained previously and apart from this study by the (CHMC) hematology laboratory for purposes of establishing normal CBC values. Venipuncture and capillary bed blood samples were drawn from 100 patients 2-10 years (6.3 years mean age) undergoing outpatient surgery who presented in good health with no apparent illness or infection as certi-

TABLE 2. Absolute Counts for Individual Leukocyte Species

	Range Cells/mm ³	\bar{x} cells/mm ³	\bar{s} cells/mm ³	% Greater Than Maximum Limit	% Less Than Minimum Limit	n	
Control							
(A) PMNs	2,520 - 6,160						
(B) Lymphocytes	1,530 - 3,740						
(C) Monocytes	180 - 440	—	—	—	—	Control population for CHMC	
(D) Eosinophils	122 - 297						
(E) Basophils	22 - 55						
(F) Band forms	135 - 330						
Group 2							
(A) PMNs	4,386 - 17,548	9,574	3,422	85.0%	0.0%		40
(B) Lymphocytes	596 - 6,096	2,433	1,164	10.0%	20.0%		
(C) Monocytes	176 - 1,782	746	397	80.0%	2.5%		
(D) Eosinophils	0 - 700	110	147	7.1%	65.0%		
(E) Basophils	0 - 162	17	42	12.5%	87.5%		
(F) Band Neutrophils	0 - 712	99	195	15.8%	82.5%		
Group 3							
(A) PMNs	2,400 - 23,331	10,595	5,065	83.3%	2.4%	42	
(B) Lymphocytes	708 - 7,261	2,859	1,420	19.0%	7.1%		
(C) Monocytes	0 - 4,480	860	822	74.8%	9.5%		
(D) Eosinophils	0 - 1,370	169	288	16.7%	59.5%		
(E) Basophils	0 - 360	15	44	11.9%	88.1%		
(F) Band Neutrophils	0 - 4,256	501	1,052	28.6%	66.7%		

fied by preoperative history and physical by an examining physician.

Blood samples in Groups 2 and 3 were obtained by venipuncture. Blood samples in Groups 1a and 1b were obtained by capillary bed sticks. Differences in CBC values for venipuncture specimens and capillary bed specimens are negligible with the exception of the hemoglobin value which is approximately 1 mg/100cc lower in venous blood than in capillary blood. The hemoglobin values collected in this study were not adjusted for this difference due to the fact that control values utilized in the study reflect hemoglobin values both for venous and capillary bed specimens collected from a large population. Platelet counts and WBC differential counts were not performed for blood samples obtained from capillary bed specimens in Groups 1a and 1b unless total WBC count exceeded 11,000 WBC/mm³. It is the policy of the hematology laboratory of CHMC to omit WBC differential counts on blood samples submitted unless total WBC count exceeds 11,000 cells/mm³ or unless specifically requested in doctor's orders. Platelet counts likewise are omitted unless specifically requested or unless accompanied by an elevated WBC count (greater than 11,000). (This is because the WBC differential count and the platelet count are not yet automated at this

hospital and must be completed manually by certified technicians.) This policy and the fact that the data in this study was gathered in retrospect accounts for the fact that WBC differential counts and platelet counts were not obtainable for patients in Groups 1a and 1b.

The data were compiled and analyzed in the following manner: maxima, minima, mean, and standard deviation were calculated for each CBC parameter for each patient in each of the four test groups. In Groups 2 and 3, absolute counts were obtained for each type of leukocyte. The absolute count for a particular leukocyte was calculated in the manner prescribed in a standard reference text.¹¹

$$\text{Absolute value for particular leukocyte in question (cells/mm}^3\text{)} = \frac{\text{Value for that particular cell (from differential count)}}{\text{Total WBC count}} \times 1/100$$

These calculations were conducted because the differential count alone rarely has any significant meaning without being interpreted in relation to the total WBC count.¹¹

Tests of significance utilized in this study were the t-test of the differences between two means and the chi-square (χ^2). Statistical significance was defined as $p \leq .05$.¹²

Results

The results are presented in detail in tabular form in Table 1. The mean age for each group was as follows: 6.3 years for the control group referenced; 6.4 years for Group 1a; 6.1 years for Group 1b; 8.4 years for Group 2; and 5.9 years for Group 3. For purposes of clarity, the results are grouped according to the various CBC tests.

Red Blood Cell Count and Indices

Mean values for the hematocrit, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were well within the normal ranges for each group.

Platelet Count

Groups 2 and 3 were well within control ranges with mean platelet count values of 337,500 platelets/mm³ and 394,250 platelets/mm³, respectively. This difference, however, was significant ($p \leq .001$).

Leukocyte Count

Two of 35 patients in Group 1a (5.7%) had total WBC counts in excess of the maximum normal limit. One of the 34 patients in Group 1b (2.9%) had a total WBC count in excess of normal. Twenty-four of 40 patients in Group 2 (60.0%) had total WBC counts in excess of normal. Thirty-one of 42 patients in Group 3 (73.8%) had total WBC counts greater than the maximum normal limits. Values lower than the minimum normal limit for the total WBC count were encountered in 2 of 35 patients in Group 1a (5.7%) and 2 of 34 patients in Group 1b (5.7%). Leukopenia was not observed in Groups 2 and 3.

The mean total leukocyte count was within-normal range for the dental caries group (Group 1a) and also for the dental caries with periradicular pathoses group (Group 1b). The dental caries group yielded a slightly higher mean WBC count than the caries with periradicular pathoses group (\bar{x} for group 1a = 7,200 cells/mm³; \bar{x} for group 1b = 7,100 cells/mm³). This difference was not statistically significant. The mean total leukocyte count exceeded the maximum normal limit in the facial cellulitis of dental etiology group (Group 2) and in the periorbital cellulitis group (Group 3). The mean total WBC count was 12,400 cells/mm³ for Group 2 and 15,000 cells/mm³ for Group 3. The mean total WBC count difference between Group 2 and Group 3 was significant ($p \leq .050$). When mean WBC counts were compared in Group 1a and Group 2, statistical significance was found at the .001 level ($p \leq .001$). The difference in the mean WBC counts for Group 1b and Group 2 also was found to be statistically significant at the .001 level ($p \leq .001$).

WBC Differential Count

The results of the WBC differential count were in-

terpreted relative to its use in calculating the absolute value of the various types of leukocytes encountered (Table 2). Granulocytes (neutrophils, eosinophils, basophils, and band neutrophils) will be discussed first followed by agranulocytes (monocytes and lymphocytes).

A. Granulocytes

1. *Neutrophilic leukocytes (PMNs)*: 85.0% of the patients in Group 2 had an absolute neutrophil count in excess of normal as compared to 83.3% for Group 3. One of 42 patients in Group 3 (2.4%) had an absolute neutrophil count below normal. There were no patients (0 of 40) in Group 2 who had absolute neutrophil counts below normal limits. The mean absolute neutrophil count for Group 2 was 9,574 cells/mm³ vs. 10,595 cells/mm³ for Group 3. These values were not statistically significant at the .05 level ($p \leq .10$).

2. *Eosinophilic leukocytes*: 7.1% of the patients in Group 2 had an absolute eosinophil count higher than normal. In Group 3 16.7% of the patients had higher than normal eosinophil counts; 65.0% of the patients in Group 2 had lower than normal eosinophil counts as compared to 59.5% of the patients in Group 3. The mean absolute eosinophil count for Group 2 was 147 cells/mm³ vs. 288 cells/mm³ for Group 3. The difference in the mean absolute count for both groups was significant at the .05 level ($p \leq .02$).

3. *Basophilic leukocytes*: 12.5% of the patients in Group 2 had absolute basophil counts in excess of normal; 11.9% of the patients in Group 3 had absolute basophil counts in excess of normal. Of the patients in Group 3, 11.9% had absolute basophil counts in excess of normal; 87.5% and 88.1% of the patients in Groups 2 and 3, respectively, had absolute basophil counts below normal. The mean absolute basophil count for Groups 2 and 3 was 17 cells/mm³ and 15 cells/mm³, respectively. This difference was not significant at the .05 level.

4. *Nonsegmented (band) neutrophils*: 27.5% of the patients in Group 2 exhibited band neutrophils in the WBC differential count as compared to 35.7% for the patients in Group 3. The mean value for the absolute band neutrophil count for all patients in Groups 2 and 3 was 99 cells/mm³ and 501 cells/mm³, respectively. Calculating the mean value for only those patients in each group who exhibited band neutrophils in the WBC differential count revealed a mean count of 357 band neutrophils/mm³ in Group 2 and 1,403 band neutrophils in Group 3 (Table 3). Calculated t-test values utilizing the mean values from all patients in both groups revealed a significant difference at the .05 level ($p \leq .0001$). The same level of confidence was obtained utilizing the mean absolute band neutrophil value for only those patients in Groups 2 and 3 who

TABLE 3. Prevalence of Band Neutrophilia in Patients With Acute Cellulitis of Dental and Nondental Etiology

	<i>N</i>	Number Exhibiting Bands In Differential Count (%)	Number exhibiting bands in Differential C Absolute Band Count 500 Cells/mm ³ (%)
Dental cellulitis	40	11 (27.5%)	3 of 11 (27.2%)
Periorbital cellulitis	42	15 (35.7%)	12 of 15 (80.0%)

actually exhibited band neutrophils in their individual WBC differential counts. Because of the difference between the two groups, the following hypothesis was advanced:

In patients with facial cellulitis who exhibit band neutrophils in the WBC differential count, an absolute count of greater than 500 band neutrophils/mm³ implies a nondental etiology; whereas, an absolute count below 500 band neutrophils/mm³ implies a dental etiology (Table 3).

The calculated chi-square was 5.66. This value proved to be statistically significant ($p \leq .025$).

B. Agranulocytes

1. *Lymphocytic leukocytes*: 10.0% of patients in Group 2 and 19.0% of patients in Group 3 had an absolute lymphocyte count greater than normal. Twenty per cent of patients in Group 2 and 7.1% of patients in Group 3 had an absolute lymphocyte count lower than normal. The differences in these percentages for the two groups were not statistically significant. However, the difference in the mean absolute lymphocyte count for Groups 2 and 3 was statistically significant ($\bar{x} = 2,433$ cells/mm³ for Group 2, $\bar{x} = 2,859$ cells/mm³ for Group 3). The mean values for each group were still well within range of normal and therefore not clinically significant.

2. *Monocytic leukocytes*: 80.0% of the patients in Group 2 had an absolute monocyte count in excess of normal as compared to 74.8% of the patients in Group 3. Of the patients of Group 2 2.5% had an absolute monocyte count below normal as compared to 9.5% of the patients in Group 3. The mean absolute monocyte count for patients in Group 2 was 746 cells/mm³ as compared to 960 cells/mm³ in Group 3. Mean values for both groups exceeded the control values for normal. This difference was not significant at the .05 level.

Body Temperature

The mean body temperature for Group 1a was 98.5°F; Group 1b, 98.6°F; Group 2, 100.2°F; and Group 3, 100.2°F. The difference in mean body temperature among the four groups showed a statistically significant

difference only between the noncellulitis groups (Groups 1a and 1b) and the cellulitis groups (Groups 2 and 3). The difference was significant at the .05 level ($p \leq .001$).

Discussion

Clinically, the findings of greatest practical significance deal with the white cell portion of the blood. Dental infection, from the stage of incipient caries to fulminant cellulitis, had no effect upon the RBC portion of the CBC. Consequently, the majority of this discussion will center on findings associated with the total WBC count, the WBC differential count, and the interrelationship between them. Body temperature and its relationship to dental infection will be discussed as an incidental finding.

Of primary importance in this study is the finding that no abnormal CBC values are encountered with dental infections until they reach the stage of acute facial cellulitis. Bacterial invasion and colonization of the teeth (caries) fails to elicit a systemic blood response as measured by the CBC. Perhaps more surprising is the fact that invasion of the periradicular area by the advancing infection likewise fails to elicit a systemic blood response. A response is seen, however, when dental infection reaches the stage of acute facial cellulitis. The characteristic responses seen in this study were: (1) neutrophilia, (2) monocytosis, (3) eosinopenia, and (4) basopenia. These findings were also true for those patients with cellulitis of nondental origin and were consistent with the WBC picture of bacterial infections in general as reported by Weitzman.⁶ There was a difference, however, with regard to the appearance of band neutrophils in the two groups of patients presenting with cellulitis. Band neutrophils appeared in the WBC differential counts of the two groups with similar frequency (27.5% for patients of Group 2 vs. 35.7% for patients of Group 3) with a slight edge going to those patients with cellulitis of nondental origin. However, comparing only those patients who actually exhibited band neutrophils in the WBC differential, the number of band neutrophils appearing per patient was radically different for the two groups ($\bar{x} = 357$ cells/mm³ for Group 2 vs. $\bar{x} = 1,403$ cells/mm³ for Group 3). It

appears from these findings that the likelihood of a shift to the left is greater in nonodontogenic cellulitis than in odontogenic cellulitis. These results also suggest that in patients with facial cellulitis, an absolute band count of greater than 500 band neutrophils/mm³ strongly implies a nondental etiology, or at least an additional contributing agent other than odontogenic infection. Therefore, in patients presenting with facial cellulitis in whom the clinical examination fails to determine the causative agent, the absolute band neutrophil count (band neutrophil fragment in the WBC differential count x total WBC count) may be of practical diagnostic importance.

The effects of dental infection on body temperature appear to duplicate the trend manifested by the hematologic reaction. Normal values for body temperature were seen in patients with caries alone and also in patients with caries plus periradicular pathosis. Only in patients with facial cellulitis was there fever. This would be expected in view of current theories on the interrelationship between leukocytosis and fever production.⁷ There was no difference in the magnitude of fever in patients with nonodontogenic cellulitis as compared to patients with facial cellulitis of dental origin.

It is beyond the scope of this study to elucidate the histologic and bacteriologic picture in the progression of dental caries from the incipient stage to its final manifestation. However, one aspect of this process will be discussed. There has been perpetual difficulty in establishing which bacteria predominate once the infectious process of dental caries involves the periradicular area. The majority of studies designed to investigate this situation have been based upon bacterial cultures taken after extraction of offending teeth. Hence, the problem of culture contamination seems inescapable. Even studies utilizing preextraction cultures taken through the root canal or through the alveolar plate reveal microorganisms generally found in the normal flora of the oral cavity. Because of this dilemma, some investigators have suggested that the dental granuloma is predominantly a sterile lesion.¹³ If this is the case for periradicular involvement of dental infection generally, it would provide an explanation for one finding of this study — namely, that the white blood cell response in patients with periradicular lesions is no different from those patients who have carious lesions without periradicular involvement.

Conclusions

Findings from this study suggest four conclusions.

1. Facial cellulitis of odontogenic origin causes a

characteristic alteration of the CBC which involves only the white cell portion of the blood. The specific findings are neutrophilia, monocytosis, eosinopenia, basopenia, and generalized leukocytosis.

2. Neither caries nor periradicular involvement causes alterations of the CBC.
3. Cellulitis of dental origin characteristically does not cause a shift to the left. If, however, immature neutrophils are encountered, an absolute band count of greater than 500 cells/mm³ implies nondental etiology or at least an additional nondental contributor to the infection.
4. In no case should laboratory values usurp clinical findings; rather, they should be used as augmentative evidence either supporting or refuting the tentative clinical diagnosis.

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