Scientific Article

Prevalence of selected pediatric conditions in children with Pierre Robin sequence

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Abstract

Pierre Robin sequence (PRS) is a congenital abnormality characterized by micrognathia and glossoptosis, with or without cleft palate. Patients with PRS may demonstrate various pediatric conditions such as associated syndromes, respiratory distress, feeding difficulties, or middle ear pathology. The purpose of this study was to determine, by means of a retrospective computerized review of patient records, the presence of these pediatric conditions in a sample of 55 confirmed patients with PRS. Five patients (9.1%) exhibited associated syndromes; 20 (36.4%) had respiratory distress requiring no assistance; and 10 (18.2%) exhibited severe respiratory distress requiring tracheotomy. A total of 30 patients (54.5%) had early feeding difficulties requiring mechanical assistance to maintain adequate nutrition, and 50 (90.9%) had multiple episodes of otitis media. Chi-square analysis revealed a statistically significant relationship between the presence of respiratory difficulties and the need for feeding assistance ($P = 0.012$); and a highly significant relationship between the presence of otitis media and subsequent myringotomy tube placement ($P < 0.001$). Pediatric dentists who treat children with PRS should be aware of these relationships when obtaining medical history before establishing strategies to implement a treatment plan. (Pediatr Dent 17:106–11, 1995)

Pierre Robin sequence (PRS) is a well-recognized congenital condition involving a combination of micrognathia and glossoptosis, with or without cleft palate. Although reports of this sequence have appeared in the literature for more than 75 years, Pierre Robin, a French stomatologist, was credited with delineating the physical components of the condition.[1]

Hanson and Smith, and Cohen suggested that the Robin defect was not a specifically delineated syndrome, but rather an "anomalad".[2,3] Further nosological changes occurred when Cohen suggested the name, Robin malformation complex. The currently accepted term for this disorder is Pierre Robin sequence.[4] The use of the word "sequence" stemmed from the observation that the micrognathic or retrognathic mandibular abnormality could lead to secondary anomalies such as the characteristic upper airway obstruction (Fig 1) and U-shaped palatal cleft (Fig 2).

It is hypothesized that abnormal embryologic development of the mandible in PRS occurs 7–11 weeks postconception, resulting in an unusually high tongue position within the nasopharynx. Concurrently, the lateral palatal shelves begin their medial growth toward the midline. However, the tongue is unable to descend due to lack of mandibular growth. The palatal shelves are obstructed by the tongue from moving toward the midline and fusing, thus creating a U-shaped palatal cleft. Generally it is believed that, after birth, an infant who is an obligate nose breather, experiences upper airway obstruction because of glossoptosis.[5]

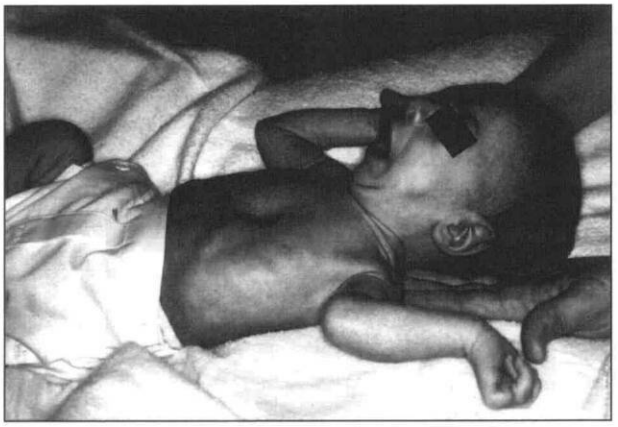

Fig 1. Infant with PRS demonstrating retrognathic mandible and respiratory distress.

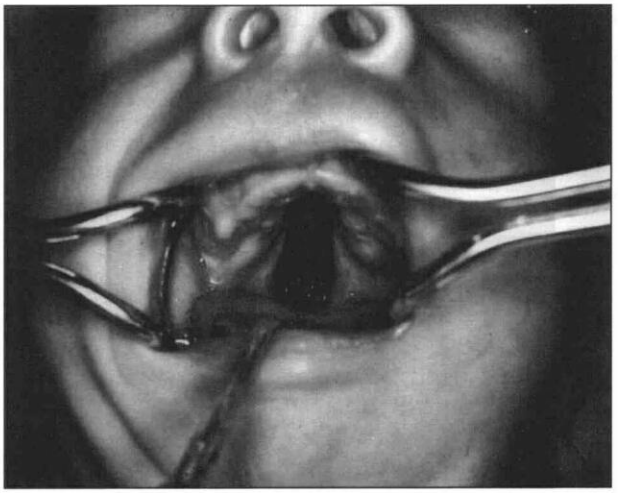

Fig 2. Same infant with PRS demonstrating characteristic U-shaped palatal cleft.

Since PRS is not a specific entity, it has neither a precise list of symptoms, nor a single etiology. The mechanisms that lead to its occurrence as well as the clinical presentation can be variable.[5] Nonetheless, the basic triad of findings consistent with a diagnosis of PRS includes: 1) micrognathia, 2) U-shaped palatal cleft, and 3) upper airway obstruction.

Shprintzen indicated that 80% of children with PRS have other abnormalities, as well as a high occurrence of associated syndromes.[6] In the Shprintzen study, 34% of patients with PRS were diagnosed with Stickler syndrome. Velocardiofacial syndrome, fetal alcohol syndrome, and provisionally unique pattern malformation syndromes accounted for an additional 31% of the PRS cases. Syndromic associations with clefting are now known to be more common than reported previously and the syndromic association of PRS is far greater than that reported for cleft lip and/or cleft palate patients alone.[6-9]

Hanson and Smith studied 38 patients retrospectively.[2] Thirty-six percent had one or more associated anomalies and 25% had known syndromes. This sample included both living and deceased subjects. In another genetic study, Sheffield et al. examined 64 patients and reported a significant proportion of cases with an underlying syndrome (34%).[10] Some of the syndromes reported in the sample include: Stickler syndrome, trisomy 18, and Treacher Collins syndrome.

In contrast, Williams et al. observed 55 PRS patients with 14 having congenital abnormalities.[11] No patient exhibited a definite diagnosis of a syndrome. Poradowska et al. reviewed the medical records of 62 newborns with PRS.[12] Forty-four percent were found to have developmental anomalies, but the researchers could not diagnose a single patient who had a recognizable syndrome.

The most acute clinical finding affecting infants with PRS is upper respiratory obstruction. It is understood that airway obstruction may not always be caused by glossoptosis, as other mechanisms have also been delineated.[13] Various methodologies have been attempted to treat airway obstruction in infants with PRS. Positioning can be appropriate for some patients. However, Sher found that positioning alone was not effective long term.[13] The use of nasoendotracheal intubation has been suggested by several authors to be the most effective method to protect the airways of infants with PRS.[13,14] Intubation times reported in the literature varied from hours to weeks. Glossopexy has been demonstrated also to be an effective treatment in select cases of obstruction caused specifically by glossoptosis.[15]

Feeding difficulties often are associated with PRS. Many professionals assume that feeding difficulties in patients with palatal clefts are related directly to the cleft, resulting in the inability of the infant to "suck". Shprintzen indicated that feeding difficulties were related more often to the airway obstruction and respiratory difficulties than to the infant's sucking ability.[6] As a result of the physical inability to separate oral from nasal cavities, newborns with PRS were required to suckle several seconds and then stop to breathe. This resulted in prolonged feeding times and more swallowed air. With upper airway obstruction, efforts of the infants were aimed primarily at maintaining a patent airway; therefore, feeding sometimes became problematic. Treatment for relief of upper airway obstruction usually resolve the feeding problems. If necessary, feeding techniques may be modified. Enlarging nipple holes, frequent burpings, and the use of compressible nursers facilitated feedings. When feeding problems became so severe that there was significant failure to thrive, tube or lavage feedings were necessary.[14]

A high incidence of middle ear difficulties has been

Table 1. Selected conditions in male patients with Pierre Robin sequence

Date of Birth	*Syndrome*	*Respiratory Problems*	*Feeding Assistance*	*Otitis Media*	*Myringotomy Tubes*
07/25/71	–	–	+	+	+
07/12/72	–	+	+	+	+
02/11/74	–	–	+	+	+
04/07/76	–	–	+	+	+
06/12/77	–	–	+	+	+
01/26/78	–	+	–	+	+
04/17/79	–	+	+	+	+
10/11/79	–	+	+	+	+
05/02/80	+	+	–	+	+
07/21/80	–	+	+	+	+
02/22/81	+	+	+	+	+
03/06/82	–	–	–	+	+
06/08/83	–	–	–	+	+
04/05/84	+	–	–	–	–
04/25/84	–	+	–	+	+
12/02/84	–	+	+	+	+
10/11/85	–	–	–	+	+
05/21/86	–	+	+	+	–
05/28/86	–	+	+	+	+
08/05/87	–	–	–	–	–
12/30/87	–	+	+	+	+
Total	3	12	13	19	18
% of total	14.3	57.1	61.9	90.5	85.7

Chi-square analysis revealed no statistically significant differences between males and females.

documented in children with palatal clefts.[16] This association was an unexpected finding that was later related to decreased pneumatization of the temporal bones.[17] Since the Eustachian tube in infants with clefts does not properly ventilate the middle ear, chronic serous otitis media is a frequent finding. If untreated, this pathologic condition can lead to a conductive hearing loss.

Pashayan and Lewis observed otolaryngologic characteristics in 25 patients with PRS.[18] These patients were divided into two groups — one with isolated PRS (N = 17) and another with PRS as part of a syndrome or associated with multiple congenital anomalies (N = 8). They found that eight of the 17 patients with isolated PRS (47.0%) and all of the eight PRS patients with a syndrome or multiple congenital anomalies had middle ear fluid. Five of the eight subjects in both groups culminated in myringotomy tube placement.

The purpose of this study was to determine the presence of selected pediatric conditions in a sample of confirmed patients with PRS. The conditions examined included:

1. Associated syndromes
2. Respiratory distress and treatment methods
3. Feeding difficulties and modifications
4. Otitis media and subsequent placement of myringotomy tubes.

TABLE 2. SELECTED CONDITIONS IN FEMALE PATIENTS WITH PIERRE ROBIN SEQUENCE

Date of Birth	*Syndrome*	*Respiratory Problems*	*Feeding Assistance*	*Otitis Media*	*Myringotomy Tubes*
04/14/72	–	+	+	+	+
07/27/73	–	–	–	+	+
09/19/74	–	–	+	+	+
12/06/76	–	–	–	+	–
08/15/77	–	+	+	+	+
10/05/77	–	+	+	+	+
11/26/77	–	–	+	+	+
08/08/79	–	+	–	+	+
09/28/79	–	–	–	+	+
09/28/80	–	+	+	+	+
07/17/81	–	+	+	+	+
01/15/83	–	+	+	+	+
05/25/83	–	–	–	+	+
06/04/83	–	–	–	+	+
06/13/83	–	+	–	+	+
10/07/83	+	+	–	+	+
01/30/84	–	–	–	–	+
06/13/84	+	–	+	+	+
07/26/84	–	–	–	+	+
11/10/84	–	+	+	+	+
01/18/85	–	+	–	+	–
01/23/85	–	–	–	+	+
02/10/85	–	–	–	–	–
04/13/85	–	+	+	+	+
08/17/85	–	–	+	+	+
01/29/86	–	+	+	–	–
06/08/86	–	+	+	+	+
08/07/86	–	–	–	+	+
10/20/86	–	+	+	+	+
12/01/86	–	+	–	+	+
04/20/87	–	+	–	+	+
10/09/87	–	+	+	+	+
10/14/87	–	–	+	+	+
12/18/88	–	–	–	+	+
Total	2	18	17	31	30
% of total	5.9	52.9	50	91.2	88.2

Chi-square analysis revealed no statistically significant differences between males and females.

Methods and materials

A retrospective computerized review of patient records at the University of Pittsburgh Cleft Palate-Craniofacial Center was conducted. All patient records with a documented diagnosis of PRS were included in this study. Verification of patients with PRS who exhibited an associated syndrome were confirmed by chromosomal analysis. General demographic information including age, race, and gender was collected as well as specific information regarding respiratory difficulties, feeding problems, and middle ear infections. Information regarding the presence of underlying syndromes also was included for analysis. The data were collected and analyzed by means of descriptive and inferential statistics using SPSS for analysis.[19]

Results

A retrospective review of all patient records at the Cleft Palate-Craniofacial Center revealed a total of 55 confirmed cases of PRS. Of these, 21 (38.2%) were male and 34 (61.8%) were female (Tables 1 and 2). No significant differences existed between male and female patients for the pediatric characteristics evaluated. Thus, the data were pooled for statistical analysis. Racial distribution revealed 53 Caucasians and only two African Americans.

Forty-six patients (83.6%) presented no evidence of underlying congenital syndromes. Two patients (3.6%) demonstrated mental retardation that was not associated with other syndromic conditions. Two subjects (3.6%) presented with an unconfirmed "suspicion" of Stickler syndrome. Sufficient

documentation was available to definitively diagnose specific syndromes in five patients (9.1%). Confirmed syndromes included:

1. Velocardiofacial syndrome
2. Wolff-Parkinson syndrome
3. Dubowitz syndrome
4. Deletion of long arm of chromosome #4
5. An unspecified #4 chromosomal disorder.

Chi-square analysis did not demonstrate any significant relationships for the presence of a syndrome and the existence of respiratory difficulties, the need for feeding assistance, the occurrence of otitis media, or subsequent myringotomy tube placement.

When respiratory difficulties were examined, 25 subjects (45.5%) demonstrated no apparent respiratory distress at birth or during the first year of life. Another 20 (36.4%) exhibited various symptoms of respiratory distress, but required no mechanical respiratory assistance. These symptoms included: six with positional respiratory difficulties (10.9%); five with unspecified respiratory distress without mechanical aids (9.1%); four with sleep apnea (7.3%); three with cyanosis when feeding or crying (5.5%); two with respiratory distress associated with birth (3.6%); and one with chronic bronchitis (1.8%). Ten patients (18.2%) exhibited severe respiratory distress requiring tracheotomy procedures to assist respiration. Tracheotomy tube placement varied from 8 hr to 29 months. None of the patients had a recorded history of aspiration pneumonia, congestive heart failure, or pulmonary edema. All patients demonstrated improved respiratory function over time, and no long-term respiratory difficulties resulted.

In terms of feeding difficulties, 25 patients (45.5%) demonstrated no reportable need for mechanically assisted feeding devices. Thirty patients (54.5%) were found to have early feeding difficulties severe enough to necessitate the use of mechanical assistance to maintain adequate nutrition. Of these, 21 patients required nasogastric or orogastric intubation for periods varying in length from 3 days to 18 months. Five patients required compressible nursers, three required custom nipples, and one required lavage feedings. Chi-square analysis revealed a statistically significant relationship between respiratory difficulties and the need for feeding assistance within this sample ($P = 0.012$).

Fifty PRS patients (90.9%) presented with multiple episodes of otitis media, while only five (9.1%) experienced no middle ear disease. The patient was considered to have otitis media if one or more of the following parameters were present:

1. Otalgia
2. Fever
3. Otorrhea
4. Recent onset of irritability.

Forty-eight patients with otitis media (87.3%) received myringotomy tube placement. Chi-square analysis revealed a highly statistically significant relationship between the presence of otitis media and subsequent myringotomy tube placement for patients in this sample ($P < 0.001$).

Discussion

Patients with PRS may demonstrate various pediatric conditions that require accurate diagnosis and medical management. Pediatric dentists, as well as other members of a comprehensive health care team, must be aware of possible relationships between PRS and various medical conditions so that appropriate dental treatment strategies can be instituted.

Several studies in the literature reported selected medical findings in patients with PRS. However, most of these studies have had relatively small sample sizes, compared with our study in which 55 confirmed patients with PRS were evaluated.[2, 18] Furthermore, many studies have utilized variable criteria for the diagnosis of PRS, while in our study, the 55 patients with PRS were all documented using the criteria of microglossia and glossoptosis.

In similar studies by Williams et al.[11] and Poradowska et al.[12], no patients were reported to have associated syndromes; however, developmental anomalies were observed. Results of our study revealed that while the majority of patients with PRS demonstrated no evidence of syndromes, five patients (9.1%) with confirmed genetic test results were diagnostic for definitive syndromes.

By contrast, Hanson and Smith[2], Sheffield et al.[10], and Shprintzen[6] all reported samples with a higher frequencies of known syndromes than did our study. In this study, only living, active patients from the Cleft Palate-Craniofacial Center were included in the analysis. Patients who may have had a syndrome in association with PRS and had died during the prenatal or neonatal period were not registered at the center and, therefore, were not included. Sheffield et al.[10] reviewed both living and deceased cases, which may explain the higher frequency of syndromes associated with PRS in that study. The rate of syndromic association in the study by Sheffield et al.[10] was higher in the deceased group (70%) than in the living group (26%). When adjusted for only living subjects, the results of our study approximate more closely those of Sheffield et al.[10] Moreover, this project recorded only patients with syndromes that had been verified by chromosomal analysis. Several of the previous studies did not use chromosomal analysis to document the presence of a syndrome.[2, 11, 12]

Respiratory difficulties appeared to be a common finding in patients with PRS. In our study, the majority of patients (54.5%) demonstrated symptoms of respiratory distress. This appeared to be a consistent finding

among studies.[13,15] The severity of the respiratory difficulties tended to determine the type of treatment utilized. In the most severe cases, tracheotomy tube placement was the treatment of choice. In this study, 18.2% of the patients required tracheotomy procedures, but none were treated with glossopexy. This study differs on the issue of glossopexy from the studies reported by Argamaso[15] and Sher.[13] In the Argamaso study,[15] 41.3% of the patients were treated by glossopexy. Sher[13] examined 53 patients, of whom 24 (45.2%) required glossopexy and nine (16.9%) required tracheotomy. Differences in the rate of tracheotomy procedures may be attributed to a regional preference in treatment philosophy. In our center, tracheotomy is the treatment of choice for advanced respiratory problems. Additionally, glossopexy appears to be a less favorable treatment option with many surgeons due to possible dehiscence formation, esthetic concerns, or functional problems with the lip or the tongue. Speech development considerations also need to be addressed if glossopexy is chosen.[15]

The majority of infants in this study with PRS required early mechanical feeding assistance to support life. Fifty-four percent were found to have early feeding difficulties severe enough to necessitate mechanical assistance to maintain adequate nutrition. Several authors have suggested modifications in feeding appliances so that sufficient caloric intake could be maintained.[6,14] Custom nursers, modified nipple design, and positional modifications were suggested as methods to aid in difficult feeding situations. Shprintzen indicated that most feeding difficulties could be attributed to upper airway obstruction.[6] In our study, a statistically significant relationship was found between the presence of respiratory difficulties and the need for feeding assistance ($P = 0.012$). Feeding problems should alert the clinician to the possible presence of respiratory problems and vice-versa.

A high incidence of middle ear difficulties has been documented in children with palatal clefts[16] as well as in infants with PRS.[18] Pashayan and Lewis reported a 64% occurrence of middle ear fluid in their sample of patients with PRS and a 62% myringotomy tube placement.[18] In our study, 90.9% of patients with PRS demonstrated multiple episodes of otitis media and 87.3% of these received myringotomy tubes. This finding represents a statistically significant relationship ($P < 0.001$) between the presence of otitis media and subsequent myringotomy tube placement. Untreated otitis media can lead to serious conductive hearing loss; therefore, it is critical to carefully monitor these patients for middle ear disease, and if present, intervene with appropriate treatment.

Despite the many medical conditions occurring in PRS patients, the long-term prognosis appears to be favorable. However, in patients with PRS who have associated syndromes, the severity of the syndromic characteristics will dictate the outcome. Because of the respiratory difficulties encountered by the majority of infants with PRS, the pediatric dentist who may be required to provide early comprehensive treatment must be aware of potential respiratory compromise when selecting the appropriate pharmacotherapeutic modalities. Caution must be exercised to maintain the patency of these airways. Since early feeding difficulties have been demonstrated to exist in patients with PRS, the pediatric dentist must accurately measure growth parameters over time to document possible growth complications such as failure to thrive, growth lag, or catch-up growth. Furthermore, the presence of a high degree of middle ear pathology and subsequent myringotomy tube placement should alert the practitioner to the possibility of conductive hearing loss or delayed speech development. The presence of the palatal cleft and subsequent surgical repair may result in posterior crossbite and a high likelihood for ectopic eruption of the maxillary first permanent molars. The micrognathic mandible, although alleviated somewhat with growth over time, may still result in the development of a pseudo Class II arch relationship requiring functional, interceptive, or comprehensive orthodontic management.

Conclusions

1. The majority of patients with PRS did not demonstrate evidence of syndromes.
2. The majority of patients with PRS experienced respiratory difficulties.
3. The majority of patients with PRS demonstrated feeding difficulties severe enough to necessitate mechanical assistance. There was a statistically significant relationship between the presence of respiratory difficulties and the need for feeding assistance ($P = 0.012$).
4. The majority of patients with PRS experienced multiple episodes of otitis media with subsequent myringotomy tube placement. There was a statistically significant relationship between the presence of otitis media and subsequent myringotomy tube placement ($P < 0.001$).

Dr. Elliott is associate professor of pediatric dentistry and head, division of administration; Dr. Studen-Pavlovich is assistant professor of pediatric dentistry; and Dr. Ranalli professor of pediatric dentistry and executive to the dean, all at School of Dental Medicine, University of Pittsburgh.

The study was supported in part by NIH Grant #DE01697 to the Cleft Palate-Craniofacial Center.

1. Cohen MM: The Robin anomalad — its nonspecificity and its associated syndromes. J Oral Surg 34:587–93, 1976.
2. Hanson JW, Smith DW: U-shaped palatal defect in the Robin anomalad: developmental and clinical relevance. J Pediatr 87:30–3, 1975.
3. Cohen MM Jr: Syndromes with cleft lip and palate. Cleft Palate J 15:306–28, 1978.

4. Jones KS, Ed: Smith's Recognizable Patterns of Human Malformation. 4th Ed. Philadelphia: WB Saunders Co, 1988, pp 196–97.
5. Sadewitz VL: Robin sequence: changes in thinking leading to changes in patient care. Cleft Palate Craniofac J 29:246–53, 1992.
6. Shprintzen RJ: The implications of the diagnosis of Robin sequence. Cleft Palate Craniofac J 29:205–9, 1992.
7. Rollnick BR, Pruzansky SJ: Genetic services at a center for craniofacial anomalies. Cleft Palate J 18:304–13, 1981.
8. Shprintzen RJ, Siegal-Sadewitz VL, Amato J, Goldberg RB: Anomalies associated with cleft lip, cleft palate, or both. Am J Med Genet 20:585–95, 1985.
9. Jones MC: Etiology of facial clefts: prospective evaluation of 428 patients. Cleft Palate J 25:16–20, 1989.
10. Shiffuekd LJ, Reiss JA, Strohm K, Gilding M: A genetic follow-up study of 64 patients with Pierre Robin complex. Am J Med Genet 28:25–36, 1987.
11. Williams AJ, Williams MA, Walker CA, Bush PG: The Robin anomolad (Pierre Robin syndrome) — a follow-up study. Arch Dis Child 56:663–68, 1981.
12. Poradowska W, Reszke S, Lenkiewica T: Pierre Robin syndrome — type and degree of developmental anomalies in 62 newborns and infants. Pediatr Pol 56:607–11, 1981. [in Polish with English abstract]
13. Sher A: Mechanisms of airway obstruction in Robin sequence: implications for treatment. Cleft Palate Craniofac J 29:224–31, 1992.
14. Singer L, Sidoti EJ: Pediatric management of Robin sequence. Cleft Palate Craniofac J 29:220–23, 1992.
15. Argamaso RV: Glossopexy for upper airway obstruction in Robin sequence. Cleft Palate Craniofac J 29:232–38, 1992.
16. Stool SE, Randall P: Unexpected ear disease in infants with cleft palate. Cleft Palate J 4:99–103, 1967.
17. Stool SE, Winn R: Pneumatization of the temporal bone in children with cleft palate. Cleft Palate J 6:154–59, 1969.
18. Pashayan HM, Lewis MB: Clinical experience with the Robin sequence. Cleft Palate J 21:270–76, 1984.
19. Nie NH et al: Statistical Program for the Social Sciences, 4th Ed. New York: McGraw-Hill, 1990, 949 p.

From the Archives

From the days of foot pedal dental drills and ineffective local anesthesia comes this paean to pain from a patient

(with indebtedness to Edgar Allen Poe)

Hear the buzzing of the drill,-
Rasping drill!
What a world of torture in my jaw it doth instill!
In this molar void and aching,
Wretched havoc it is making.
I am gagged; I cannot speak,
I can only shriek, shriek, shriek, In a clamorous
appealing to the mercy of the dentist,
In a mad expostulation with the
fierce malicious dentist,
Digging harder, harder, harder,
With a savage fiendish ardor,
And a resolute endeavor,
Now to slay me, now or never,
Oh, the drill, drill, drill.
How it files and scrapes and grates!
How it grinds and triturates!
In the whirring and the burring
Does my anguish sink and swell,
In the crushing and the cutting of the drill,
Of the drill, drill, drill, drill,
Drill, drill, drill-
In the punching and the crunching of the drill!
Hear the humming of the drill,
Wicked drill!
What a world of agony its clatterings foretell!
Through my blood a chill 'tis sending
With its sing-song never ending.
In the harness, bit and rubber,
I can only slobber, slobber.
And to make things more like Hades,
through the window can I see
The devil on the court-house leering
viciously at me.
While the drill is gritting, gritting,
And my frantic nerves are splitting,
My defenseless flesh is crawling
'Neath the friction hot and galling.
Oh, the drill, drill, drill;
How it scratches, pounds and thumps!
How it spins and bores and bumps!
Keeping time, time, time,
In a sort of Runic rhyme
To the rapping and the tapping of the drill,
Of the drill,
Of the drill, drill, drill, drill,
Drill, drill, drill,
To the ramming and the cramming of the drill!

Sarah Van Buskirk, The Dental Summary, 1904