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A
s many of us will be gathering around a table this Thanksgiving, may we all take a moment to give thanks for all our blessings to include the opportunity to be in our profession of medicine. And, for all those who have taught us and led us, may we offer a moment of special thanks.

Over the course of the last year, we have lost some significant teachers and have also become aware of health challenges to others we hold dear. To you and your families, may this upcoming holiday season find you well and enjoying the blessings of togetherness that this season promotes. May we honor our medical family as well.

As physicians, we are currently facing a number of changes (and challenges) to include: the implementation of electronic health records (EHRs) and ICD-10; the implementation of a value-based future payment model using untested payment methodologies; balancing our patient caseload so that we ensure the delivery of quality health care without negatively impacting patient access; and an ever seemingly erosion of the time we have to dedicate to taking care of our patients. I recall that analogy of the round table of fabled King Arthur, where his knights gathered to protect his people and promoted that familiar saying of “right makes might.” Some days it seems to play out as “might makes right.”

Addiction and the abuse of prescription medications is currently a hot topic, even prompting a letter from the U.S. Surgeon General in which he called on all physicians to be diligent and thoughtful. I anticipate that federal guidelines on prescribing are forthcoming while our nation faces this crisis. However, in doing so, we cannot forget to address the contributing problems of mental health and pain, both acute and chronic. Simply cutting back or restricting a physician’s ability to prescribe medications for pain will not in and of itself solve the problem of prescription drug abuse. As we strive to reduce prescription drug abuse, we must also look at coverage issues, limitations or economic barriers to specialty care, and patient compliance.

Homelessness, poverty, and hunger continue to challenge our society and our profession, and so before we can improve the health of the people of our country, we must also address these contributing factors. I would also go so far as to say that science and advances in medical technology alone cannot improve public health – and sometimes, we are our own worst enemies. Individual freedom of choice, and well-intended social guidance supported by scientific information, are often at odds. What our society often considers embracing our freedoms is often at odds with our laws. The legalization of medical and recreational marijuana despite our lack of scientific support for its safe use is one example; the ability to exempt your child from mandatory vaccines due to personal reasons is another.

While many of us have heard that a significant percentage of health care dollars are spent on a much smaller percentage of patients, we also know that living a life of proper diet and exercise, and routine/preventive health care can prevent chronic conditions and reduce the cost of health care. Thinking back to King Arthur and the round table in which “right makes might,” I can’t help but envision the future in another way – “a circle of care.” In this model, the patient is in the center with a protective circle comprised of care management and health care providers who also advocate for sound public policies that contribute to both the health and financial well-being of patients. To be successful, it would require us to embrace the team approach to care, and to also work together to advocate for sound public policy that improves both access to care and coverage.

May we as physicians be grateful for the opportunities to practice medicine and may our “circles of care be unbroken,” because it might just seem right.
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In the busy world of medical education, it is hard sometimes to take a step back and look at the big picture. The University of South Dakota Sanford School of Medicine (SSOM) receives a lot of data each year comparing our school to national averages. One parameter is board examination results. Students take three national board examinations in medical school and another board examination in the beginning of their residency. These boards are administered by the United States Medical Licensing Examination (USMLE) organization.

Step 1 of the USMLE focuses on basic science and its clinical applications. The test evaluates how well the student understands the mechanisms of health, disease, and treatment. Step 1 is traditionally taken at the end of the basic science curriculum, which is what we call Pillar 1. Our Pillar 1 curriculum is carefully designed to provide foundational science content that is integrated with clinical concepts, and to accomplish this in an efficient time frame. Thus, SSOM students take Step 1 a few months earlier than most students in the country. The effectiveness of the curriculum, skill of the faculty, and the exceptional work of the students is reflected in our recent pass rate. Of SSOM students, 96.5 percent passed Step 1 on their first attempt. National data are not yet available for this year, but in 2015 it was 95 percent nationally.

Step 2 of the USMLE has two parts. The Clinical Knowledge (Step 2 CK) examination seeks to evaluate understanding of clinical components including clinical reasoning. In the most recent report of students who took the examination from June 2015 to July 2016, 99 percent of our students passed on the first attempt compared to a national average of 96 percent. Again, our students took the test earlier in their medical school training than most of the rest of the country yet they exceeded the national passing rate. One major advantage of the curriculum is that residency programs can see our students’ Step 2 CK scores prior to selecting candidates to interview. For most other students in the country, residency programs must rely solely on Step 1 results because applicants from other schools have not yet received their scores from Step 2 CK. This gives our students an advantage because programs are receiving far more applications than in the past, and our students’ Step 2 CK results can demonstrate their clinical competence to prospective residencies, whereas their competitors do not have scores in hand. It is one factor that contributed to our great match results: 100 percent of our students got a residency slot this year, with 98.4 percent matching on the first computer run and the remainder finding a slot on the second run. None of our students had to scramble to find a residency slot outside of the computer-based system. The national match rate for U.S. medical graduates was 93.8 percent for the first computer run.

Step 2 also has a part called Clinical Skills (Step 2 CS). This is an off-site examination where students evaluate standardized patients and are judged on their ability to take a history, do a physical examination, communicate with patients and write a cogent note. There is growing frustration nationwide with the relevance of this exam and the related expenses borne by students, as has previously been described in South Dakota Medicine (August 2016). Our most recent results show that 100 percent of SSOM students passed Step 2 CS on the first attempt compared to 96 percent nationally.

Step 3 of the USMLE is taken early in residency. It is designed to evaluate whether a student has the knowledge required for unsupervised practice. Our most recent data show that 100 percent of our students passed Step 3 on the first try compared to a national average of 97 percent.

These are outstanding results. Board pass rates at SSOM across all boards exceeded national averages as did our residency match rate. This combination of results places SSOM among the top schools in the nation. The results are a testament to the SSOM curriculum and especially to the excellent work of the faculty and students who make up the school.
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An Exciting Time to Practice Internal Medicine

The field of biomedical informatics is changing the way we deliver health care. Through the widescale expansion of electronic medical records (EMRs), automated decision support is increasingly being used to reduce risk and optimize quality. Some risk prediction models now include genetic factors, and patients are beginning to ask us for help understanding the impact of their genome on their overall health within the context of routine clinical care.

Primary care is well positioned to help our patients navigate this transformation. However, primary care providers are increasingly being pressured to optimize throughput, and their experience with the emerging field of genomics is highly variable. As a community, we need to position our providers for success, by making sure they have access to the information that they need without compromising their efficiency in the context of a busy practice. In this issue of South Dakota Medicine, Evenson et al. report their efforts to begin defining the area of greatest need.

Nearly 90 percent of internal medicine providers surveyed by Evenson indicate an understanding that genetic factors influence every aspect of disease management (i.e., prevention, diagnosis, and treatment). However, only half of these providers feel confident explaining genetic test results. Further, there appears to be a mismatch in their comfort level discussing genetic predictors of disease and genetic predictors of drug response. Only one-fourth of the providers surveyed by Evenson’s team were comfortable fielding questions about genes and disease susceptibility.

Clearly we have our work cut out for us. One proposed approach to this challenge has been the integration of genetic counselors in primary care clinics. As practice groups explore team-based models of health care delivery, this approach seems desirable, and the findings reported by Evenson confirm that providers have a strong willingness (88 percent) to expand the role of genetic counselors in their day-to-day practice. This is an exciting time to practice internal medicine, and multidisciplinary teams (nurses, pharmacists and geneticists) will play a role in our success.

– Russell A. Wilke, MD, PhD, FACP, Professor and Chair, Department of Internal Medicine, University of South Dakota Sanford School of Medicine.
Abstract

Introduction: The convergence of biomedical informatics and translational genomics is changing the way we practice. Primary care will play a pivotal role in this transformation. We therefore sought to assess general knowledge about genetic testing among outpatient internal medicine providers, and the patients that they serve across a five-state region in the Midwest.

Methods: One thousand take-home paper surveys were created and distributed to internal medicine patients at 13 Midwestern clinics. Sixty-two electronic surveys were also created and distributed to internal medicine providers at these same clinics. Questions assessed knowledge, interest, and comfort with genetic testing as well as the role of genetic counselors. Differences in response based on physician characteristics were compared using a Chi-squared analysis.

Results: In general, patients cared for in internal medicine clinics expressed an understanding of both content (75 percent) and rationale (81 percent) for genetic testing. Patients are open to hearing about genetic risks that could affect their health (88 percent) even if their visit was scheduled for a different reason. In these same clinics, providers expressed a strong understanding of the purpose of genetic testing (88 percent). However, providers were not confident in responding to questions about the impact of genetic testing on disease susceptibility (25 percent). Providers were more confident answering questions about genetic variability in drug response (46 percent). In general, outpatient internal medicine providers feel comfortable referring patients to genetic counselors to assess disease risk (88 percent) and they believe genetic testing is relevant to their practice (75 percent).

Conclusion: In our Midwestern sample, we found that both patients and providers express interest in learning more about genetic testing in the context of primary care. Patient and physician responses indicate a role for genetic counselors in helping our patients understand and interpret genetic test results.

Introduction

Genetic testing is a rapidly growing field that is an important part of modern health care and is increasingly important for primary care. Yet, there are potential obstacles to any program that attempts this integration of genetic testing and primary care, including patient and physician reception and response. While there have been studies that investigate how patients or physicians perceive and understand genetic testing in either a limited, disease-specific example or in a prospective manner, none have been able to monitor what these perceptions are and how they change during the course of a genetic testing primary care program.

In 2014, a program was started with internal medicine physicians to incorporate genetic testing in their clinics. The program spans 13 internal medicine clinics across South Dakota, North Dakota, and Minnesota, and looks to progressively install pharmacogenetic testing. To do so, the program started with educational sessions for physicians prior to implementation. Also, on-site genetic counselors are being integrated into clinics to provide aide for physicians in explaining genetic test results. The program thus allows a unique look into how patient and physician perspectives change over the course of a genetic testing program and further assesses the readiness of patients and physicians for this step in health care.

The literature suggests that patients and physicians are open and interested in genetic testing. Patients have been found to largely approve of genetic testing and are interested in its use in primary care. This support has been shown to be high when patients have a specific chronic disease. Receiving a genetic test helped patients at risk for a chronic disease to feel less anxious, and patients have shown a desire for their children to undergo genetic testing to understand risk for that chronic disease. Those with a chronic disease show a greater interest in genetic testing if their disease correlates with a family history of that disease.

The literature also suggests the use of genetic counselors to help patients understand their genetic testing results. Patients often need direct support in making sense of
genetic information.8 Also notable, patients have been found to be concerned about the safety and use of their genetic data.5

Studies on primary care physicians’ views strongly suggest that they are interested in and support the incorporation of genetic testing in primary care settings.4,9 At the same time, however, physicians often lack the knowledge to feel comfortable with the utilization of genetic test results.8,9-11 This lack of physician knowledge and comfort is true for both pharmacogenetic testing and genetic testing for disease risk.4,11 Studies have thus stated the need for better education of primary care physicians on incorporating genetic testing into their practices before starting such a program.4,9,11 Those physicians who feel they have more knowledge about genetic testing agree more strongly that genetic testing will have a significant impact on their future practice.11 Specific to pharmacogenetics, primary care physicians are undereducated and recognize this, but they still see pharmacogenetics as a valuable tool to be used by primary care physicians in the future.4,9

This study examines baseline data on patient and physician perceptions of genetic testing in a primary care setting. The goals are to examine perceived knowledge and comfort with genetic testing so as to inform future efforts for integrating genetic testing in primary care. Future research will compare how survey respondents’ views change compared to this baseline data.

Methods

Surveys were created for internal medicine patients and physicians and distributed at 13 Midwestern clinics across South Dakota, Minnesota, and North Dakota. This study was institution based and the sites involved were chosen because of their involvement in integrating the genetics program. Surveys were created by identifying areas that the authors felt were of significance when querying genetic testing perceptions. Then, questions were tailored for each area. Questions were reviewed by content experts including a clinical geneticist, a genetic counselor, and other genetic researchers. This study was approved by the institutional review boards at the University of South Dakota and Sanford Research as an exempt study.

Patient surveys were distributed at the end of a patient’s visit to an internal medicine physician. Patients were instructed to take the survey home, fill it out, and return it in a self-addressed, stamped envelope. The survey elicited information about patient demographics and medical conditions and included questions about the patient’s knowledge of genetic testing, perception of usefulness of genetic testing and concerns, and interest in genetic testing. Also, privacy concerns were investigated by asking patients their concerns broadly about their genetic data and specifically about privacy from insurance or employers. A total of 1,000 patient surveys were distributed. The number of patient surveys was chosen based on an expected 20 percent response rate for estimating confidence intervals for proportions with widths lower than 15 percent. The number of surveys provided to each clinic was based on the total number of internal medicine physicians.

Physician surveys were distributed through a web-based survey tool to all 62 internal medicine physicians practicing at the 13 clinics. Although ideally these surveys would have been distributed prior to the program’s educational sessions, due to timing restrictions we were unable to distribute it until midway through this program. Reminders to complete the survey were sent weekly for one month. The surveys included questions about physician knowledge and understanding of genetic testing – the process, the purpose – how confident they feel communicating with patients about genetic testing results, their perceptions on the relevance of genetic testing in their practice, how genetic testing relates to preventative healthcare, and how they feel about the role and use of genetic counselors. In the physician surveys, genetic testing was broadly defined as including pharmacogenetics, disease susceptibility, or disease diagnosis.

These physician surveys also included three short case studies that asked physicians to respond to situations involving genetic testing. Specifically, these case studies looked at how physicians value pharmacogenetic and genetic testing information versus patient response to medications when the two do not agree. Also, physicians were queried on how they would respond if asked for a predictive genetic test, specifically on Parkinson’s disease due to the weight of such a request.

Data was then analyzed using descriptive methods including frequency and percentages. Component scores were created by a combination of iterative splitting and factor analysis using the VARCLUS procedure in the SAS software. Cronbach’s alpha was calculated for each cluster. Questions with low correlation within each cluster were removed and the analysis was redone. Total scores were calculated for each component by average individual question responses and dichotomized due to the limited
distribution (less than four; greater than or equal to four). Analysis of differences in component scores by demographic information was performed using Fisher’s exact test. Sensitivity analysis was also conducted for the patient survey after weighting the data based on the patient population for the 13 clinics. All analysis was performed using SAS software, version 9.4.

Data was secured throughout the process using a number of different methods. Hard copies of surveys were stored in a locked filing cabinet accessible only by study staff. Data from the mailed surveys was transferred directly to an electronic database by a single individual and stored on a secure server in a password-protected relational database accessible only by study staff. Restrictions on the entry possibilities of data elements were added to improve data quality. Physician surveys were electronic and downloaded into a secure database. If patients or physicians did not answer a question within the overall survey, that survey question was not included in the final results but the rest of their survey responses were included.

Results
Patient Surveys
The response rate for the patient surveys was 14 percent. Demographics of the sample are presented in Table 1. The majority of respondents were white (99 percent) females (74 percent) with some college education or greater (83 percent), married (79 percent), and aged 50 to 79 years old (77 percent). Most patients lived in a city with a population greater than 50,000 (51 percent), although close to one-quarter lived in towns less than 2,500 (19 percent). Incomes were varied with over half reporting an income over $60,000 (52 percent).

The majority of patients reported that they see their internal medicine doctor regularly for some disease (66 percent) with the most common being arthritis (46 percent) and diabetes (23 percent). Four components were identified including knowledge, benefit/interest, openness, and concern (Table 2). Patients were generally knowledgeable (46 percent), interested in genetic testing (66 percent), open to hearing about genetic testing (84 percent), and did not have concerns that would cause them to not have genetic testing done (5 percent) (Figure 1). However, a sizeable portion noted worry about keeping their genetic test results private generally (31 percent) and specifically as it

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>White</td>
<td>131 (98.5)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>Yes</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>132 (99.2)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>34 (26.0)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>97 (74.0)</td>
</tr>
<tr>
<td>Education</td>
<td>High school or less</td>
<td>23 (17.4)</td>
</tr>
<tr>
<td></td>
<td>Some college</td>
<td>35 (26.5)</td>
</tr>
<tr>
<td></td>
<td>College degree</td>
<td>43 (32.6)</td>
</tr>
<tr>
<td></td>
<td>Graduate/professional school</td>
<td>31 (23.5)</td>
</tr>
<tr>
<td>Age</td>
<td>18-49</td>
<td>17 (12.9)</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>29 (22.0)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>37 (28.0)</td>
</tr>
<tr>
<td></td>
<td>70+</td>
<td>49 (37.1)</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married</td>
<td>104 (78.8)</td>
</tr>
<tr>
<td></td>
<td>Divorced</td>
<td>13 (9.8)</td>
</tr>
<tr>
<td></td>
<td>Widowed</td>
<td>7 (5.3)</td>
</tr>
<tr>
<td></td>
<td>Never married</td>
<td>8 (6.1)</td>
</tr>
<tr>
<td>Location</td>
<td>City with a population &gt;50,000</td>
<td>67 (50.8)</td>
</tr>
<tr>
<td></td>
<td>Town, population between 10,000 and 50,000</td>
<td>25 (18.9)</td>
</tr>
<tr>
<td></td>
<td>Town, population between 2,500 and 9,999</td>
<td>15 (11.4)</td>
</tr>
<tr>
<td></td>
<td>Town, population &lt; 2,500 or in the country</td>
<td>25 (18.9)</td>
</tr>
<tr>
<td>Income</td>
<td>Up to $40,000</td>
<td>33 (25.8)</td>
</tr>
<tr>
<td></td>
<td>More than $40,000 up to $60,000</td>
<td>29 (22.7)</td>
</tr>
<tr>
<td></td>
<td>More than $60,000 up to $80,000</td>
<td>28 (21.9)</td>
</tr>
<tr>
<td></td>
<td>More than $80,000</td>
<td>38 (29.7)</td>
</tr>
</tbody>
</table>

Some percentages may not equal 100 due to rounding.
concerns their insurance or employer (14 percent). Also, more patients agreed that a genetic counselor could teach them about genetic testing (78 percent) compared to their primary care doctor (56 percent) (p = 0.01). No statistically significant differences in component scores by demographic or medical factors were observed. Results were similar when adjusted using non-response weights based on clinic wide distribution of patients by gender and age.

Physician Surveys

The response rate for the physician surveys was 42 percent. The majority of respondents were male (58 percent), all between ages 30 to 69, and were divided in years of practice, with most either having 0 to five years (39 percent) or over 20 years (39 percent) in practice (Table 3). The majority (73 percent) of physicians had not ordered a genetic test in the past 6 months or had never ordered a genetic test (54 percent) (Table 3).
Four components were identified including knowledge, confidence, relevance, and use of genetic counselors (Table 4). While 67 percent of physicians were in the high knowledge category, only 21 percent were in the high confidence category (Figure 2). Relevance scores were split with 46 percent indicating that genetics testing was highly relevant to their practice. Most also had high comfort levels in working with genetic counselors (54 percent), were generally knowledgeable, open to hearing about genetic testing, interested in genetic testing, and did not have concerns that would cause them to not have genetic testing. Although not categorized with the other questions, most physicians felt that genetic testing would lead to advances in preventative health care (75 percent). Overall knowledge was significantly higher for those who had ever ordered a genetic test (46 versus 91 percent, p= 0.03). No other differences reached statistical significance.

Case studies were presented to see how physicians would respond to situations involving genetic testing. While there was some variation in responses, most physicians agreed that if a genetic test showed a patient to be a poor metabolizer of a particular medication then it should be changed (78 percent). Agreement was lower on just changing the dose of the medication rather than the medication itself (23 percent). If approached by a patient whose medication was not addressing her symptoms, despite the drug being well suited for her condition and genetic testing supporting proper metabolism of the drug, most physicians disagreed that the patient should continue the drug (64 percent) and believe the patient should switch to another drug (70 percent). Lastly, if a patient has a family history of Parkinson’s disease and wants to know if he or she is at an increased risk for

---

Table 4. Physician Component Groups Definition and Responses

<table>
<thead>
<tr>
<th>Group</th>
<th>Question</th>
<th>Disagree</th>
<th>Neither</th>
<th>Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge Alpha = 0.78</td>
<td>I understand the process of genetic testing.</td>
<td>2 (8.3)</td>
<td>6 (25.0)</td>
<td>16 (66.7)</td>
</tr>
<tr>
<td></td>
<td>I understand the purpose of genetic testing.</td>
<td>0 (0.0)</td>
<td>3 (12.5)</td>
<td>21 (87.5)</td>
</tr>
<tr>
<td>Confidence Alpha = 0.86</td>
<td>I feel confident in communicating genetic test results to my patients.</td>
<td>8 (33.3)</td>
<td>6 (25.0)</td>
<td>10 (41.7)</td>
</tr>
<tr>
<td></td>
<td>I am comfortable in responding to my patients’ questions regarding genetic testing as it relates to drug response.</td>
<td>6 (25.0)</td>
<td>7 (29.2)</td>
<td>11 (45.8)</td>
</tr>
<tr>
<td></td>
<td>I am comfortable in responding to my patients’ questions regarding genetic testing as it relates to disease susceptibility.</td>
<td>4 (16.7)</td>
<td>14 (58.3)</td>
<td>6 (25.0)</td>
</tr>
<tr>
<td>Relevance Alpha = 0.73</td>
<td>Genetic testing is an important tool in my ability to care for patients.</td>
<td>3 (12.5)</td>
<td>9 (37.5)</td>
<td>12 (50.0)</td>
</tr>
<tr>
<td></td>
<td>Genetic testing is relevant for my practice.</td>
<td>1 (4.2)</td>
<td>5 (20.8)</td>
<td>18 (75.0)</td>
</tr>
<tr>
<td>Genetic Counselors Alpha = 0.92</td>
<td>I would refer my patients to genetic counselors for questions on genetic testing.</td>
<td>0 (0.0)</td>
<td>3 (12.5)</td>
<td>21 (87.5)</td>
</tr>
<tr>
<td></td>
<td>I would refer my patients to genetic counselors for information about familial implications of genetic testing.</td>
<td>0 (0.0)</td>
<td>3 (12.5)</td>
<td>21 (87.5)</td>
</tr>
<tr>
<td></td>
<td>I understand what a genetic counselor does.</td>
<td>0 (0.0)</td>
<td>8 (33.3)</td>
<td>16 (66.7)</td>
</tr>
<tr>
<td></td>
<td>I am comfortable working with a genetic counselor.</td>
<td>0 (0.0)</td>
<td>6 (25.0)</td>
<td>18 (75.0)</td>
</tr>
<tr>
<td></td>
<td>I understand the scope of practice of a genetic counselor.</td>
<td>3 (12.5)</td>
<td>10 (41.7)</td>
<td>11 (45.8)</td>
</tr>
<tr>
<td>Not categorized</td>
<td>There is value in having a genetic counselor physically working in the same clinic.</td>
<td>0 (0.0)</td>
<td>6 (25.0)</td>
<td>18 (75.0)</td>
</tr>
<tr>
<td></td>
<td>Genetic testing will help advance preventative health care.</td>
<td>0 (0.0)</td>
<td>6 (25.0)</td>
<td>18 (75.0)</td>
</tr>
</tbody>
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Some percentages may not equal 100 due to rounding.

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Figure 2.
Parkinson’s, the vast majority would refer the patient to a genetic counselor (87 percent), but not order a genetic screening test for their patient (41 percent) or are undecided on such a test (50 percent).

Discussion
As genetic testing is progressively incorporated into primary care settings in the future, health care providers will look to programs such as the one described here. Our baseline data on patient and physician perceptions of genetic testing indicate that there is an interest in genetic testing in primary care, specifically in internal medicine clinics. We found that patients were knowledgeable, had an interest in, and were open to hearing about genetic testing. Our data also suggested that patient concerns about genetic testing were not a significant barrier. Physicians had a high level of knowledge about genetic testing and this knowledge was increased for those who had ever ordered a genetic test. We also found that physicians had low levels of confidence in communication with patients about genetic testing. However, physicians were comfortable working with and referring patients to genetic counselors to provide patient education.

These results generally align with the literature on patient and physician perceptions on genetic testing. Our results bolster the idea that genetic testing would be accepted among patients and physicians, although there is a need for greater physician education on genetic testing, clinical genomics, and the role of genetic counselors. Also, as seen in the literature, our results suggest genetic counselors do have a clear role to play in the implementation and use of genetic testing in a primary care setting.

There were limitations to our study. Only internal medicine clinics in the Midwest were sampled. While one thousand patient surveys were sent to clinics, only 14 percent responded. Our response rate may have been hindered by the requirements of the clinics to not provide the surveys prior to the visit or during it.

In addition to these limitations, there were also differences in our sample based on age and gender, but not race or ethnicity. We employed a sensitivity analysis to weight the sample by population proportions and results were similar. However, this approach assumes that those who responded represent a random sample from the age and gender group and we were unable to adjust for income or education level since this data was not available for the population of clinic patients. It is possible that both income and education levels were higher in our sample than the general population and this may have influenced results. Physician response rate was better, at 42 percent, but limited in that the number of physicians who responded totaled 26.

Our data collected prior to the start of a program seeking to integrate genetics into primary care will allow us to compare how perceptions by patients and physicians change during full implementation of this program. As advancements in genomics and genetic testing progresses and our understanding grows, genetic testing will continue to be integrated into health care. Our study suggests that internal medicine patients and physicians are ready for the use of genetics in primary care, potentially paving the way for more personalized preventative healthcare.

Acknowledgements
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About the Authors:
Samuel A. Evenson, BA, MS III, University of South Dakota Sanford School of Medicine.
H. Eugene Hoyme, MD, Chief Academic Officer and Chief of Genetics and Genomic Medicine, Sanford Health, Sioux Falls, South Dakota; Professor, Department of Pediatrics, University of South Dakota Sanford School of Medicine.
Jan E. Haugen-Rogers, PhD, RN, Vice President, Imageneics, Sanford Health, Sioux Falls, South Dakota.
Eric A. Larson, MD, Physician, Sanford Health, Sioux Falls, South Dakota; Associate Professor, Department of Internal Medicine, University of South Dakota Sanford School of Medicine.
Susan E. Puurma, PhD, Associate Scientist, Center for Health Outcomes and Prevention Research, Sanford Research, Sioux Falls, South Dakota; Associate Professor, Department of Pediatrics and Department of Internal Medicine, University of South Dakota Sanford School of Medicine.
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An Unusual Presentation of an Unusual Disease: Spontaneous Pneumomediastinum

By Kalyan Chakravarthty Potu, MD; Maheedhar Gedela, MD; Kashif Abbas Shaikh, MD; Sujithasree Ketineni, MBBS; and Eric Larson, MD

Abstract
We report a case of spontaneous pneumomediastinum with unusual clinical presentation. The most common symptoms of spontaneous mediastinum are chest pain and shortness of breath. Our patient presented with neck swelling and change in voice, an unusual presentation for spontaneous pneumothorax.

A 30-year-old previously healthy man presented with complaints of neck swelling and hoarseness of voice beginning after an intense coughing spell. He had no other complaints. He denied any trauma to the chest, nausea, vomiting, recent air travel, scuba diving or recreational drug use. His vital signs were stable with an O2 saturation of 97 percent on room air. Chest examination was remarkable for palpable crepitus over lower neck as well as bilateral upper and mid anterior chest. Chest radiograph as well as chest computed tomography (CT) demonstrated a massive pneumomediastinum with free air dissecting throughout the soft tissues of the neck. The patient was admitted for observation. Neck swelling and hoarseness of voice resolved in less than 24 hours with conservative management of cough. He was discharged without incident.

Spontaneous pneumomediastinum is an uncommon, self-limiting condition in which air is present in the mediastinum with no obvious precipitating factor. Cough, inhaled drugs, physical exercise, labor, and diabetic ketoacidosis have been reported to trigger spontaneous pneumomediastinum. Our patient developed the condition after an intense coughing spell following smoking cessation. CT scan is considered gold standard for the diagnosis. Spontaneous pneumomediastinum is characterized by spontaneous recovery and can be treated with short period of observation and symptomatic management.

Introduction
Pneumomediastinum is a clinical condition defined as air in the mediastinum and may be caused by a catastrophic event, like chest trauma, esophageal rupture after vomiting, or gas producing organisms.1,2 The approximate incidence is one in 30,000 emergency department referrals.1 Spontaneous pneumomediastinum is an uncommon but mostly benign finding usually occurring in young patients with no history of an obvious precipitating factor.1 It occurs commonly in males with male to female ratio of 8:1.4 The most common symptoms are chest pain and shortness of breath. The most frequent physical signs are subcutaneous thoracic emphysema and subcutaneous cervical emphysema.5 Spontaneous pneumomediastinum may be commonly misdiagnosed because the most common presenting symptoms, chest pain and shortness of breath, occur with several other more common cardiopulmonary pathologies.4

Case Presentation
A 30-year-old previously healthy man was admitted with complaints of neck swelling and hoarseness of voice beginning after an intense coughing spell. The patient developed worsening cough after smoking cessation 2 weeks prior to presentation. He denied any trauma to the chest, nausea, vomiting, recent air travel, scuba diving or recreational drug use. The past medical history was negative for asthma or other chronic medical conditions. He had an 11 pack-year smoking history and worked in construction with exposure to concrete dust. On physical examination, the patient’s respiratory rate was 16 breaths per minute with an O2 saturation of 97 percent on room
air. Patient had no dyspnea. Chest examination was positive for palpable crepitus over lower neck as well as bilateral upper and mid anterior chest. Lungs were clear to auscultation bilaterally. Chest radiograph as well as chest computed tomography demonstrated a massive pneumomediastinum with free air dissecting throughout the soft tissues of the neck (figures 1-4). There was no pneumothorax. The patient was admitted for close observation and symptomatic management of cough. No oxygen therapy was given, as his oxygen saturation was within normal range on room air. Neck swelling and hoarseness of voice resolved in less than 24 hours with conservative management of cough. The patient was discharged without incident after 24 hours of close observation.

Discussion
Spontaneous pneumomediastinum is an uncommon, self-limiting condition in which air is present in the mediastinum with no obvious precipitating factor.\(^9\) Cough, inhaled drugs, physical exercise, labor, diabetic ketoacidosis, and others, have been reported to trigger spontaneous pneumomediastinum.\(^12\) Our patient developed the condition after an intense coughing spell relating to smoking cessation. Chronic smoking can increase number of abnormal cilia which could not participate in effective clearance of tracheobronchial secretions.\(^13\) The waking up of stunned cilia following smoking cessation could contribute to cough due to enhancement of previously ineffective tracheobronchial clearance.

The pathophysiology of spontaneous pneumomediastinum requires a three-step process involving alveolar rupture, gas dissection through the broncho-vascular fascia, and pulmonary interstitial spread to the mediastinum.\(^7,8\) The specificity of chest X-ray for diagnosis of spontaneous pneumothorax was found to be approximately 90 percent.\(^14\) CT scan is considered gold standard for the diagnosis of spontaneous pneumomediastinum.\(^15\) Spontaneous pneumomediastinum is characterized by spontaneous recovery without any specific treatment and can be treated with short period of observation and symptomatic treatment.\(^10,11\)

Conclusion
Spontaneous pneumomediastinum is an uncommon, self-limiting condition in which air is present in the mediastinum with no obvious precipitating factor. It usually occurs in young patients. The most common symptoms of spontaneous mediastinum are chest pain and shortness of breath. Our patient presented with neck swelling and change in voice, an unusual presentation for
spontaneous pneumomediastinum. Cough, inhaled drugs, physical exercise, labor, and diabetic ketoacidosis have been reported to trigger spontaneous pneumomediastinum. Our patient developed the condition after an intense coughing spell relating to smoking cessation.

**REFERENCES**


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**About the Authors:**

Kalyan Chakravarthy Potu, MD, Resident, Department of Internal Medicine, Sanford School of Medicine, University of South Dakota, Sioux Falls, SD
Maheedhar Gedela, MD, Resident, Department of Internal Medicine, Sanford School of Medicine, University of South Dakota, Sioux Falls, SD
Kashif Abbas Shaikh, MD, Resident, Department of Internal Medicine, Sanford School of Medicine, University of South Dakota, Sioux Falls, SD
Sujithasree Ketineni, MBBS, Intern, Department of Internal Medicine, Sri Venkata Sai Medical College, Andhra Pradesh, India
Eric Larson, MD, Associate Professor, Department of Internal Medicine, Sanford School of Medicine, University of South Dakota, Sioux Falls, SD
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The Seventh District Medical Society and Alliance wish to thank Dr. Wilson and Rose Asfora for opening up their restaurant, Carnaval Brazilian Grill, to host the district’s annual fall kickoff October 3.

The meal was superb, and the fellowship between students, residents, physicians and spouses made it an enjoyable evening for all.
Embracing a Deep Peace in My Soul: The Father of Autism and Treatment of the Insane in South Dakota

By Henry Travers, MD, FACP

Early infantile autism, the Department of Pediatric Psychiatry at the Johns Hopkins Hospital, and the Human Services Center in Yankton – to paraphrase *Twilight Zone* creator Rod Serling – met in space and time through an immigrant Jewish physician of Austrian birth in the mid-1920s. At a time in Germany when a health insurance strike benefitted physicians’ incomes and rampant post-war inflation had just begun to stabilize with the introduction of the Rentenmark, Leo Kanner (pronounced CONNER) dragged his family “…to the desolate prairie and arctic climate of the Dakotas.” His decision to come owed much to the central characteristic of his life – adaptability – a trait that would, as we shall see, serve him well in his adopted United States.

Kanner, born Chaskel Leib Kanner in 1894, was poised to become a university professor and Privatdozent when he learned of the “wonders of life in America” from Dr. Louis Holtz of Aberdeen, South Dakota, in a manner that “…made our mouths water…” Dr. Holtz, who was studying electrophysiology in Germany at the time, secured a position for Kanner at the State Hospital in Yankton. Kanner hedged his bets a bit, arranging only a year’s leave of absence from the district medical officer (Bezirksartz), but he and his family nonetheless embarked for America about two months after the imprisonment of Adolph Hitler for treason following the so-called Beer Hall Putsch.

Kanner spoke no English and had no special training or interest in psychiatry. In fact, he had just transferred to a gastroenterology department a few weeks prior to his departure for America. His cousin in Germany questioned his sanity for removing his family to the American interior “…where gangsters shot people down in the cities and hostile Indians roamed in open spaces.” Would he want his child “…brought up amidst savages who, after going completely insane, carried on in the asylum in which [Kanner’s family] were going to live?” While he had second thoughts, Kanner felt bound by his word to Dr. Holtz.

Politics and Insanity

In the Germany from which Kanner came, the Weimar Republic was just beginning to reestablish Germany’s economy and social order. The Republic was opposed by several small paramilitary groups, angry at the provisions of the Treaty of Versailles, who took advantage of simmering German nationalism. Anti-semitic and anti-capitalist, one of these groups, the National Socialist German Workers Party (Nationalsozialistische Deutsche Arbeiterpartei), captured leadership of the nationalist movement under Adolph Hitler from 1920 to 1923. Following the party’s unsuccessful *coup d’état* in Munich in early November 1923, Hitler was imprisoned, but the party’s principles had already frightened some Jews who believed the Nazis were not just a political fad.

During his medical training, Kanner was exposed to the teachings of pioneer psychiatrists, led by Emil Kraepelin, who had championed a biological basis for mental illness and stressed humane care and careful observation of the insane. Sadly, Kraepelin and others also subscribed to a theory of genetic degeneration, an underpinning both of their support for eugenics and the ethos of racial purity pursued by the Nazis. The combination of political power and scientific distortion led, ultimately, to the ghastly wartime treatment of the mentally ill in Germany under Kraepelin’s successor, Ernst Rüdin.

One hundred and fifty years earlier, during the French Revolution, an entirely opposite outcome was realized,
based on principles of Liberté, égalité and fraternité. Philippe Pinel in *A Treatise on Insanity* (translated by D.D. Davis, W. Todd, Sheffield, 1806, p. 48) recognized that humane treatment and true appreciation of disease were mutual necessities: “Those precepts are only of partial utility, as long as the nosology of the disease is not established upon clear and extensive views of its causes, symptoms and varieties.”

At both the Bicêtre and later at the Salpêtrière in Paris patients were give physical freedom, useless therapies were discarded in favor of observation and drugs were avoided. Pinel’s work and that of Esquirol⁵ forty years later considered insanity as a very broad spectrum of disorders. To Pinel’s mania, melancholia, dementia and idiocy were added hallucinations, social alienation and epilepsy among others, all diagnoses which could lead to involuntary institutionalization.

In spite of progress over the latter half of the 19th century and first quarter of the 20th, most everyday practitioners in the U.S. understood mental illness in terms described by Pinel and Esquirol. For that and other reasons, improved understanding of mental illness, advanced by Kraepelin, Sigmund Freud⁶ in Austria and by Adolph Meyer⁷ in the U.S. did not automatically lead to better care for the mentally ill.

Dakota Territory had early recognized the need to care for the insane, the legislature forming, in 1870, a Committee on Benevolent Institutions. Nine years later, although with a personal investment of over $2,000 by Gov. William Howard (later reimbursed), the legislature established the Dakota Hospital for the Insane in Yankton. Twenty years thereafter, in 1899, Congress created the Canton Asylum for Insane Indians in Canton, South Dakota, the only federal institution for insane Indians in the U.S.

Societal benevolence aside, the fate of persons labeled “insane” hinged on definitions of insanity, public perceptions of the insane and their families, the changing body of scientific knowledge that can be applied in the diagnosis and treatment of patients, available physical facilities, the dispositions of individual care givers and, most unfortunately, politics. While the work of European physicians previously mentioned and Dorothea Dix in the U.S. ended the banishment of the mentally ill from the human family, their treatment remained largely custodial and often under cruel conditions. Elizabeth Jane Cochran, writing under the pen name Nellie Bly, exposed not only rampant misdiagnosis, but dreadful living conditions in the Women’s Lunatic Asylum in New York;⁸ Clifford Beers⁹ published an account of his own mistreatment at a private sanatorium in the same state.

Back in Dakota Territory, the Dakota Hospital for the Insane (hereinafter referred to as the Yankton Asylum)

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6. Freud left Austria in 1938 to escape the Nazis and died the following year in exile in Britain.
7. Meyer was born in Switzerland and came to the U.S. in 1904, eventually becoming the “dean” of American psychiatrists.
8. Bly, Nellie. *Ten Days in a Madhouse*. Ian L. Munro, New York, 1887. Steven Foster wrote a popular song about her (“Nellie Bly! Nellie Bly! Bring de broom along….”). Bly wrote for the Pittsburgh Dispatch and Foster was a “favorite son” of the city.
admitted its first patient, William Bernard. His insanity was regarded as hopeless. As described by Kingsbury:10 “Bernard’s mania developed while in the Black Hills and induced him to obtain money or other valuables under false pretenses, then dispose of the other valuables and pocket the proceeds. Evidently a serious case, possibly contracted by exposure to contagion.”

He, and others like him, were cared for under the supervision of a Board of Trustees appointed by the governor. The board’s core trust was to manage the Yankton Asylum with a view to restoring its patients to their normal healthful mental and physical conditions. It became clear to many then – and with implications to our present day difficulties with the mental health examination of those in South Dakota’s jails – that politics would make compliance with that trust difficult. One of the first to recognize this was the Rev. Joseph Ward, pastor of the Yankton Congregational Church and one of the Yankton Asylum’s first trustees under Gov. Howard. He resigned in 1883 “…when he found that the affairs of the hospital were to be made a football of politics” (see footnote 10, page 1308).

In 1887, trustees appointed by Gov. Church included three Democrats and two Republicans. They worked closely with Drs. Potter (the steward, after whom Potter County was named) and Cravens (the superintendent), and Yankton Asylum management was widely considered entirely satisfactory. The governor’s “confidential friends,”11 recognizing Potter and Cravens as Republicans, promoted an “investigation” of the Yankton Asylum leading the governor “…to gather enough from the report upon which to base a pretext for refusing to approve the plans12 for improvement while the present board remained in control of the hospital” (see footnote 10, page 1479). This imbroglio continued for some months until the two Democratic trustees resigned and Gov. Church suspended the Republicans. The latter, in turn, refused to recognize the authority of the governor. Church, nonetheless, appointed a new board and the old board sued. They lost; within a year the Yankton Asylum was staffed entirely by Democrats.

Similar political machinations involved the Canton Asylum for Insane Indians (hereinafter called the Canton Asylum), although on a federal level. Legislation for its construction was introduced in the U.S. Congress by Sen. Richard F. Pettigrew who was motivated by the commercial opportunity it offered for South Dakota rather
than by an interest in insane Native Americans. The Canton Asylum was managed by the Bureau of Indian Affairs. Its first physician, Dr. John F. Turner, reflecting French psychiatric influences, classified the first 15 patients as chronic epileptic dementia, alcoholic dementia, senile dementia, congenital epileptic idiocy, congenital imbecility, acute melancholia, chronic melancholia and chronic mania. Although, for much of its existence, it had a psychiatrically trained superintendent, Dr. Harry Hummer, the Canton Asylum’s history was marked by continuing investigations of its personnel and the care they rendered.13

Dr. Hummer, in contrast to Kanner at the Yankton facility, took no professional advantage of the opportunity he was given to advance psychiatry and in 1929 he “…was maintaining the same type of patient records that he had kept since 1909; they revealed very little about the patients and their diseases.”14 In spite of overwhelming evidence of maltreatment and management incompetence collected over at least a decade, the House of Misery that was the Canton Asylum continued to function, supported by the citizens of Canton and South Dakota’s congressional delegation (Peter Norbeck, William J. Bulow and Fred H. Hildebrant), until 1934. There may be no better illustration of Osler’s observation that “…the unfortunate affiliation of insanity with politics is still in many States a serious hindrance to progress” than the Canton Asylum.15

Leo Kanner in South Dakota
It was into this milieu that Dr. Kanner arrived alone at the Yankton Asylum in February 1924. Shown to his quarters on the third floor of the administration building by the steward, Mr. Randall G. Ryan,16 Kanner, true to the requirements of citizens in Germany, sought to register his presence with the local authorities. With the help of the asylum telephone operator, he received his first lesson in American freedom from a German-speaking schizophrenic patient: “Nobody… had to be catalogued by the police… and all that was expected of you was that you did not make a public nuisance of yourself.”

Kanner and the asylum’s superintendent, Dr. George

13. There was no change in the treatment of Canton Asylum patients even though Congress, in 1924, passed the Snyder Act giving all Native Americans U.S. citizenship.
16. Ryan had come to the Yankton Asylum just a month before Kanner. He was previously steward at the South Dakota Penitentiary. He resigned his position in June 1926 (see 19th Biennial Report of the Superintendent of the Yankton State Hospital, 30 June 1926, State Board of Charities and Corrections).
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Sheldon Adams, got along well from their first meeting and were friends until Adams’ death in 1944. Adams had no psychiatric training either, coming to the Yankton Asylum in 1901 at the age of 25 and becoming superintendent in 1920. The man he replaced, Dr. L.C. Mead, was the fourth superintendent since the excitement of 1887, but he initially lasted for only three months in 1891. He subsequently became the sixth post-1887 superintendent in 1901 and served for 19 years. 17

Adams venerated American leaders in psychiatry: Meyer, William White and Abraham Brill. His grasp of their basic concepts, though, was “meager.” In fact, he believed psychiatric illness was due to focal infection and that surgery could sometimes remove the inciting infected organ (teeth, the gallbladder, the colon) and cure the affliction. Kanner recalled his teacher, Adolph Meyer, commenting on the efficacy of Bayard Holmes’ colectomies for the cure of schizophrenia: “…colons were changed to semicolons.”

Nearly all of the Yankton Asylum’s medical staff were untrained in psychiatry. The exceptions included Dr. Ina Moore-Freshour and Dr. Faris Pfister who had both trained at St. Elizabeths Hospital in Washington. Kanner noted that all “…physicians needed was a diploma from a medical school; they became ‘psychiatrists’ by dint of their employment in a mental hospital.” These physicians “…learned to look erudite when they cast their vote on whether a patient ‘had’ dementia praecox, manic-depressive psychosis, paranois, general paresis, senile, alcoholic, epileptic, or ‘undiagnosed’ psychosis. Even this was more than most universities had taught them.”

Kanner’s description of the Yankton Asylum provided a glimpse of living conditions and the types of patients housed there. There were admission houses for men and women, the latter (now called the Mead Building 18 ) with a marble stairway and Sistine Madonna. On the second floor of the men’s house were “…a select number of quiet, well-mannered, dignified men whose demeanor made it difficult for a layman to believe that they were ‘insane.’ Not one of them had been able to get along on the outside…but, removed from the responsibility for their own transaction, settled down to brood, read, doodle, play cards, and rock in their chairs.” Two cottages were open for “…those who could enjoy full liberty of the grounds, help on the farm, in the dairies…and were sufficiently contented to leave one with the assurance that they would not run away.” Two buildings, one for men and one for women, were for the aged and infirm and each had separate quarters for patients “…who ranted, soiled themselves, tore their clothes, and needed constant supervision.” A “stone room” was reserved for a “…wax museum of motionless catatronics and a bedlam of grimacing, shouting, grunting, spitting human debris.” One ward was for psychotic, dangerously aggressive criminals. In addition to these facilities, there was a pavilion five miles northeast of the hospital on the James River which could house 28 patients who would spend “…a week’s vacation from their regular routine and could indulge in the pleasures of swimming, fishing and boating.”

The initial admissions questionnaire for each patient included orientation to time, place and person; the ability to repeat words rapidly such as “Methodist Episcopal;” subtracting 7 from 100 to 0 and other simple tests of cognitive function. Beyond this, Kanner began to extensively interview patients and their relatives, reading

17. In Kanner’s manuscript he says that Mead was superintendent for 29 years, citing 1891 as the beginning of his tenure. This was historical carelessness on Kanner’s part.
Kanner questioned the psychoanalysis of Freud, contributed to – but later rejected – the psychological analysis of literary characters such as Peer Gynt, and embarked “…on opportunities for active research which presented themselves in a state hospital as if on a silver platter.” He did not support the hospital practice of establishing diagnoses based on a majority vote of the caregivers, although he went along with it.

Disturbed by the number of patients in straitjackets, in “muffs and cuffs,” or isolated in rooms, Kanner ordered the restraints removed and spent Christmas day of 1924 on the wards as a safeguard against any emergency that might arise from his order. The day passed without incident and the patients “remained unfettered.” Taking an idea from Prinzhorn’s 1922 book Die Bilderei der Geisteskranken (The Artistry of the Mentally Ill), he developed a museum for patients’ art and published a description of it in The American Journal of Psychiatry in 1926. He experimented with epinephrine injections in his patients in a study of the autonomic nervous system in psychoses. His studies challenged the earlier ideas of Hans Eppinger and Leo Hess which suggested an unbalanced relationship between sympathetic and vagal influences in psychoses; Kanner viewed the involved physiology as homeostatic.

Not all of Kanner’s professional practices represented pioneering versions of what would become mainstream psychiatry. He seized upon Julius Wagner-Jauregg’s work on malaria inoculation as a treatment for general paresis.20 His first patient, a garage mechanic from Sioux Falls, had to be transported to Rochester, Minnesota, since it was the nearest location where malarial blood could be obtained. Permission of the governor was required to remove an “insane” person from the state. Duly inoculated and monitored through the required 10 episodes of “chills,” the mechanic was pronounced cured after his return to Yankton. Soon all the hospital’s paretic patients who showed “any promise whatever” were treated. Oddly, Kanner never described the overall results of the treatment.

Wishing to gain standing as an American physician, Kanner applied to take the South Dakota licensing examination in 1925. As his application was being processed, the South Dakota Legislature passed a law prohibiting examination of foreign medical graduates until they became U.S. citizens.21 Kanner wondered “…whether laws such as these were mild manifestations of xenophobia which in less tranquil times has been known to grow to pathologic proportions.” Dr. Adams’ intercession with the South Dakota Attorney General resulted in the law being ruled unconstitutional, placing Kanner at the center of a cause célèbre.22 It would take about 18 months before Kanner was invited to take the examination in Pierre, but with only one day’s notice. He arrived late and missed all but one of the examiners who, after escorting Kanner about the capital and inviting him to the movies,

19. Hans Prinzhorn in 1919 at the University of Heidelberg expanded the collection of art by the mentally ill which was begun, not surprisingly, by Emil Kraepelin.
20. Wagner-Jauregg won the 1927 Nobel Prize in Physiology or Medicine for his work. While malaria was abandoned as a general therapy, other treatments (e.g., electroconvulsive shock) based on the general theory behind its efficacy remain in use today.
21. In 1920 about 100 foreign (excluding Canadians) physicians were examined annually by state medical boards. In 1924 the number jumped to 500 annually. State medical boards expressed concern and state legislatures responded (Johnson, DA and Chaudhry, HJ. Medical Licensing and Discipline in America, Lexington Books, Lanham, 2012, p. 90).
22. The term was Kanner’s. The Yankton Press and Dakotan carried no articles in 1925 related to Kanner’s licensing issue. It was a banner year, though, for causes célèbre: controversies over a state-owned gasoline corporation, the Scopes “monkey” trial, the delivery of diphtheria antitoxin to Nome Alaska (honored in the Iditarod race) and the court-marshal of Colonel Billy Mitchell occupied much of the pages of the Press.
finally allowed him to take the examination, unmonitored, in his hotel room the next day. He passed.

While Kanner became a U.S. citizen as soon as he was able, the solemn experience was not without its humor. He observed that Americanization consisted “…of memorizing the three great tenants that it’s not the heat but the humidity, that New York City is a nice place to visit but not live in, and that with a car it’s not the original cost but the upkeep that counts.” He recognized America as a republic of free people “…whose sense of loyalty to their country called for an aversion to any kind of autocratic regimentation.”

After four years in Yankton, during which he bought a car, joined the Masons, wrote a treatise on the folklore of teeth and learned to play poker, Kanner began dreaming of being in an active teaching center. His wife, June, was tired of living in the hospital and of having much of her family’s daily life controlled by the social order there. She gave her husband an ultimatum in spring of 1928: leave soon or she and their daughter, Anita, would move to Chicago until he secured a better position. Fortuitously, the American Journal of Psychiatry carried, in May 1928, an announcement for a psychiatry fellowship at the Henry Phipps Psychiatric Clinic at the Johns Hopkins Hospital directed by Adolf Meyer. Kanner applied, and, in due course, was accepted. As he departed from Yankton, and, consonant with his childhood ambition to make his living from poetry, he wrote:

The world before me is like a dream
Reality moved far away,
And far away moved all greed,
And every gulf is bridged.

Gold shines dim on pillars. The room
Enlightened magically and tender.
Is everything really only a dream
And this world a pale vision?

Around me a peculiar frame
Of warm gold and glimmering red.
I am an old Atheist
And proclaim it aloud: Oh, God!

Kanner and his family arrived in Baltimore on Oct. 28, 1928.

Those Tight Straitjackets of Our Striving Mind

There is very little written about Leo Kanner, including his own autobiographical work that contains an uncomplimentary word. Highly regarded as a pioneer in pediatric psychiatry, the “father” of autism, full of wit and broadly interested in history, music and literature, this naturalized American citizen, licensed to practice medicine in South Dakota until his death in 1981, is universally spoken of with great reverence. A respected school (Johns Hopkins), an association (the American Psychiatric Association) and a hospital (the Human Services Center at Yankton) are among repositories of Kanner lore in the U.S. and are jealous guardians of his legacy. Nonetheless, Kanner’s career contains some curious inconsistencies, and even the signature human disorder for which he is best known – autism – was possibly not his alone.

Three of these inconsistencies are found in his Yankton...

24. Translated from the original German by Henry Travers, MD, and Professor Utz Merten, Köln, Germany. The poem evokes some images of the architecture of the Yankton Asylum.
25. A line from an unpublished play written by Kanner. The main character was Elisha ben Abuyah, a fictional Talmudic sort whom Kanner spent years developing.
years. First, his interest in the mentally ill as individuals appeared to exclude those most seriously psychotic. While his unpublished autobiography contains numerous stories of specific patients told with interest and concern, his choice of patients to describe was selective. They all had stories to tell and were able to tell them. Only when one of those Kanner described as “human debris” became (temporarily) nearly normal did Kanner record his case. The rest of the ‘debris’ remained unmentioned in their “stone room.”

Second, he failed to report his results with malaria treatment of paretics. This omission in his autobiography contrasts with his inquisitive nature and propensity for prolific publication. One might speculate that, perhaps, the treatment generally was not so successful or that, as was the case with about 15 percent of patients treated with malaria infection, too many died of the cure.

Finally, he did nothing about the Canton Asylum. When he came to the Canton Asylum to meet the visiting Emil Kraepelin (who was studying general paresis among Native Americans), he took no action on his observations of the facility. Kanner found: “Most of the patients were either mute or spoke some Indian language; no relatives were interviewed and not even perfunctory examinations were made. Two buildings, one for men and one for women, were unsanitary. Gloom and filth were spread all over the place…”

Kanner knew Dr. H.R. Hummer, the disingenuous superintendent of the Canton Asylum; he knew what the facility was like and how differently its patients were treated from those in his own facility. He knew medical practices were substandard and he knew physicians in the Indian Health Service who could do something about them. Yet he did nothing except arrange for a microscope to be brought to Canton for Dr. Kraepelin’s work.

In 1937, nearly 10 years after leaving South Dakota, Kanner had a similar opportunity to intervene for the welfare of institutionalized mentally disabled people. An unscrupulous Baltimore lawyer was obtaining writs of habeas corpus from a cooperative judge for “feebleminded” female residents of the Rosewood State Training School. These women the attorney would offer to wealthy matrons as cheap and disposable domestic labor. Left on the streets as “vegetables” at random when they proved unsatisfactory in the households of the wealthy, the women were jailed, became prostitutes, or died. Kanner’s presentation to the American Psychiatric Association on such shenanigans gained for Kanner a nationwide image as heroic crusader for the vulnerable. The image, however, did not match an ugly reality: capitalizing on the fame and moral influence he held, he claimed that the children born to these women were “uncontestably feeble-minded” giving a powerful, if misguided, justification for eugenic practices.26

In his recent book A History of Autism (Wiley-Blackwell, United Kingdom, 2010, pages 22-40), Adam Feinstein presents an assertion that Kanner’s seminal publication on autism in 191728 drew conclusions from the unattributed previous work by Hans Asperger. The bases for the contention are weak and are characterized by “I think,” “must have heard,” and “pretty certain,” but there is no hard evidence of plagiarism. Asperger’s initial paper describing his own patients was published in 1944,29 a year after Kanner’s. It is, however, a fact that Asperger is not mentioned in Kanner’s textbook Child Psychiatry through 1957. Moreover, Kanner, well versed in psychiatric literature in both the U.S. and Europe, did not mention either Asperger or an earlier researcher, Grunya Sukhareva29 in any of his autism papers. Finally, there is documented evidence that Asperger wrote about autism (he called it “autistic psychopathy”) in professional correspondence and spoke of it in his lectures as early as 1934 (see Feinstein). Kanner and Asperger never met, even though Asperger visited the U.S.

Asperger, like Kanner, was Austrian and both were educated in Vienna. While both wrote poetry and were interested in the mental diseases of children, the similarity ends there. Asperger kept his own company while Kanner published widely and appreciated the attention he received. In a poetic eulogy for himself, Asperger wrote:

As a human being, misunderstood,
as a poet, tolerated at best,
I drag my monotonous life away.26

It appears that Asperger’s relative obscurity until his

26. Silberman, Steve. NeuroTribes: The Legacy of Autism and the Future of Neurodiversity. Random House, NY, 2015. While Silberman points out that Kanner was a public opponent of eugenics, his motivation for engaging in public debates on the subject may have been more to showcase himself than to defend the defenseless. 
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“rediscovery” by Wing in 1981\textsuperscript{10} (her paper was published in February 1981; Kanner died two months later) may have something to do with his omission in the Kanner canon.\textsuperscript{31} Even though there is simply no satisfactory explanation why Kanner, usually generous with his affection for respected colleagues, omitted Asperger from his professional life, speculation ranges from ignorance to suspicion that Asperger sympathized with the Nazis and conducted his practice accordingly. Based on available evidence (see Feinstein and Wolff), neither seems likely.

Although humor was an important part of Kanner’s persona, he sometimes used it as ridicule as the following examples illustrate. When the dining arrangements for Kanner’s daughter made by the clinical director’s wife at the Yankton Asylum caused the Kanners’ concern, Kanner circulated a parody both in the Asylum and within the town of Yankton. In it, he referred to the clinical director’s wife as the queen, a perfect tyrant, who was portrayed as exercising authority way above her station. The relationship between the clinical director and his wife and the Kanners was thereafter “…at below zero temperature.” A few years later, at Johns Hopkins, Kanner commented to the audience after Paul Schilder’s formal lecture at Johns Hopkins about the hypothalamic influences on glucose metabolism and sexual behavior, that he now understood why people called each other “honey” or “sugar” since the two hypothalamic areas involved with each were so close (Feinstein).

Summary
Leo Kanner, a lifelong autodidact, contributed profoundly to our understanding of mental illness in children. Since most of his South Dakota patients were adults and there is no indication in his description of the South Dakota years that he had any specific interest in the mental health of children, his memorable achievements in that field were the fruits of his adaptability. Indeed, had his first U.S. posting been the Mayo Clinic, Kanner may have become a giant in another medical field entirely.

His view of himself, expressed in his writings about his Yankton years, coincided with those of his colleagues, collaborators and students: there appeared to be no body of water on the planet that he could not cross on foot.\textsuperscript{32} Even though two who have written about his life recently (Feinstein and Silberman) do not sugar-coat episodes in his career, neither do they explore what these may tell us about Kanner as a person.

Kanner reveled in recognition and wasted no time in activities that brought him none. Did he actively conceal events or beliefs that either did not fit his public image or would bring recognition to others? His portrayal of his time in Yankton contains three examples that suggest he did. Describing a group of Yankton Asylum patients as “human debris,” Kanner writes about only one who temporarily recovered enough to make a good story. Exulting in meeting the revered Dr. Kraepelin visiting at the Canton Asylum,\textsuperscript{33} he mentions the appalling conditions there as a sideline to his service to the great professor and the publication which came therefrom.\textsuperscript{34} Finally, he treated all patients with general paresis at the Yankton Asylum by inducing malaria, but did not publish his results.

After Kanner left South Dakota there were additional episodes that support his preoccupation with public image and recognition. His professional neglect of Asperger, his apparent disregard for the progeny of persons judged “feeble minded” while basking in the limelight of public misperception of his role as their champion, and his sometimes mean-spirited humor could, at worst, indicate an ego incapable of accepting and promoting a self that was less than perfect.

Nonetheless, Kanner improved the lot of his young patients, established and advanced the field of child psychiatry, helped Jewish professionals escape from Nazi Germany and comforted parents confused by psychobabble and guilt. Taken together, the events of his life show a picture of Kanner the person like any of the rest of us, part in sunlight and part in shadow.

Acknowledgement
The author gratefully acknowledges the assistance of Dr. David Bean for suggesting the topic and for providing a copy of a portion of Dr. Kanner’s unpublished autobiography and Carla Joinson for both providing some background materials regarding the Canton Asylum and for editorial suggestions about the manuscript. Thanks also to Susan Kudera for providing copies of the biannual reports of the superintendent of the Yankton Asylum.

About the Author:
Henry Travers, MD, FACP; Clinical Professor of Pathology, University of South Dakota Sanford School of Medicine; Historian, South Dakota State Medical Association.
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Current Guidelines on Syncope

By Maheedhar Gedela, MD; Naveen Rajpurohit, MD; Kashif Shaikh, MD; Muhammad Omar, MD; and Scott Pham, MD

Abstract
Syncope is a very commonly encountered clinical problem in general practice and in the emergency department. In the evaluation of syncope, it is important to identify the specific cause to determine the treatment, to estimate the precise risk to a patient, and to reduce recurrence. Sometimes, making a diagnosis of syncope is difficult, as different mechanisms may often coexist. Syncope causes a significant impact on quality of life due to associated risk of physical injury. In particular, syncope can be a precursor to sudden cardiac death in patients with underlying cardiac disease. It is crucial to identify patients at increased risk of death, such as those with myocardial ischemia and/or potentially life-threatening genetic diseases (e.g., Long-QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and arrhythmogenic right ventricular dysplasia). After these conditions have been excluded, other benign conditions that cause syncope must be identified, and efforts should be made to improve quality of life. The lack of a gold-standard clinical tool to aid in diagnosing syncope as well as improper use of various diagnostic tests, are leading to high economic burdens in this area.

Introduction
Syncope accounts for approximately 1 percent of emergency department visits. Reflex syncope is the most common cause of syncope in the general population. The most common cause of sudden cardiac death (SCD) in adolescents is hypertrophic cardiomyopathy. Various age-related physiological changes in the elderly predispose them to syncope. Nearly 30 percent of falls suffered by the elderly may be due to syncope. Importantly, in the elderly, multiple origins of syncope often coexist. In the U.S., the estimated total annual costs for syncope-related admissions are $2.4 billion, with a mean cost of $5,400 per hospitalization. Incidence of syncope rises with age, from 5.7 events per 1,000 person-years in men aged 60 to 69 to 11.1 in men aged 70 to 79. Syncope is defined as a transient loss of consciousness that is characterized by rapid onset, brief duration, and spontaneous complete recovery. Pre-syncope or near syncope commonly contains various symptoms of lightheadedness, nausea or visual disturbances that occur prior to the onset of syncope, but is not followed by loss of consciousness (LOC). A sudden cessation of cerebral perfusion as short as six to eight seconds is sufficient to cause LOC. The term LOC is very broad and includes syncope along with subsets such as epileptic seizures, concussion, psychogenic pseudosyncope, cataplexy, several metabolic disorders (e.g., hypoglycemia and hypoxia), and coma. An overlap exists between falls, orthostatic hypotension, and dizzy spells, which may all present as syncope. It is very important to differentiate syncope from other subsets of LOC to limit diagnostic confusion.

Classification of Syncope
It is very complex and challenging to classify syncope, as most of its categories are based on overlap and the combination of various pathophysiological processes rather than a single mechanism. However, a distinction common in these pathophysiological processes is transiently decreased cerebral blood flow due to a drop in blood pressure (BP). BP is determined by cardiac output (CO) and systemic vascular resistance (SVR). A drop in either CO or SVR or a combination of both (although their relative contributions vary) can cause syncope. The classification of syncope based on pathophysiology is shown in the illustration.

Reflex syncope (neurally mediated syncope) is caused by a failure of the cardiovascular reflexes to respond normally to triggering situations such as emotions, micturition, defecation, carotid sinus massage, or post-exercise. “Vasovagal” syncope, also known as “common fainting” falls under this category.
Orthostatic hypotension (OH) is defined as an inappropriate decrease in systolic BP upon standing. There are several categories under OH based on the time from standing to the onset of symptoms. “Classical OH” occurs within three minutes of standing. In “initial OH”, the period of hypotension and symptoms is brief, usually less than 30 seconds. OH can be subdivided into primary autonomic failure (e.g., Parkinson disease, Lewy body dementia, and multiple system atrophy), secondary autonomic failure (e.g., diabetes and amyloidosis), and drug-induced OH (e.g., vasodilators and diuretics).

Cardiac rhythm disturbances (e.g., tachy-brady syndrome and atrioventricular conduction system defects) are the most common cause of cardiogenic syncope, followed by structural heart disease (e.g., aortic stenosis and atrial myxoma).

Evaluation of Syncope
A detailed clinical history and physical examination, including orthostatic BP and electrocardiogram (ECG), should be obtained for a patient presenting with LOC. In 23 to 50 percent of cases, this initial evaluation reveals most of the causes of syncope and permits the institution of specific treatment. The initial questionnaire should gather information on circumstances prior to the attack (e.g., change in position, emotional stress, coughing spells), prodromal symptoms (e.g., nausea, aura, sweating), eyewitness details, duration of the episode, and symptoms following the attack (e.g., confusion, chest pain). Auras, forewarning symptoms, postictal confusion, and focal neurological signs suggest a neurological cause. Carefully noting a history of unexplained SCD in the family, previous heart disease and neurological problems, metabolic disorders, and medications can aid in the diagnosis of

Table 1. High-Risk Features Requiring Immediate Hospitalization or Intensive Evaluation

<table>
<thead>
<tr>
<th>CLINICAL FEATURES</th>
<th>ECG FEATURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Heart failure</td>
<td>• Prolonged or short QT interval</td>
</tr>
<tr>
<td>• Low left ventricular ejection fraction</td>
<td>• Pre-excited QRS complex</td>
</tr>
<tr>
<td>• Previous myocardial infarction</td>
<td>• Non-sustained ventricular tachycardia</td>
</tr>
<tr>
<td>• Family history of SCD</td>
<td>• Brugada pattern (right bundle branch pattern with ST elevation in leads V1-V3)</td>
</tr>
<tr>
<td>• Palpitations at the time of syncope</td>
<td>• Arrhythmogenic right ventricular cardiomyopathy (negative T waves in right precordial leads, epsilon waves)</td>
</tr>
<tr>
<td>• Syncope during exertion or when supine</td>
<td>• Inadequate sinus bradycardia (&lt; 50bpm) in absence of negative chronotropic medications or physical training</td>
</tr>
</tbody>
</table>
syncope and prevent further expensive evaluations. In patients younger than 40 years of age, a drop in BP or failure of BP to rise with exercise raises the possibility of hypertrophic obstructive cardiomyopathy or left main coronary artery disease.\(^{12}\) When OH is suspected, a manual recording of BP when supine and during active standing for three minutes is beneficial. If the patient has a symptomatic drop in systolic BP greater than or equal to 20 mm Hg or diastolic BP greater than or equal to 10 mm Hg or a decrease in systolic BP to less than 90 mm Hg, then it is considered diagnostic for OH.

Additional testing is necessary to assess the risk of major cardiovascular events or SCD if the cause of syncope remains unclear after the initial evaluation.\(^{13,14}\) Important high-risk clinical and ECG features are shown in Table 1.

**Carotid sinus massage** – In patients over the age of 40, carotid sinus massage (CSM) is recommended if there is no diagnostic clue after the initial evaluation.\(^{15}\) CSM is considered diagnostic if syncope is reproduced in the presence of ventricular pause longer than three seconds and/or a fall in systolic BP more than 50 mm Hg. CSM is contraindicated in patients with previous transient ischemic attacks or stroke within the past three months, or with carotid bruits.

**Tilt testing** – If reflex syncope is not revealed with the initial evaluation, tilt table testing is beneficial to confirm its diagnosis.\(^{16}\) Tilt table testing is useful in patients with a single, unexplained syncope in high-risk situations, such as an occurrence of, or potential risk of, physical injury or occupational implications. It is also recommended in recurrent episodes of syncope in the absence of structural heart disease, or in the presence of structural heart disease after the cardiac etiology of syncope has been excluded. Tilt testing can be provoked pharmacologically through a low-dose isoproterenol infusion or sublingual nitroglycerin.

**Non-invasive and invasive electrocardiographic (ECG) evaluation** – ECG monitoring is considered only when there is a high probability of finding an arrhythmia as a cause of syncope. In patients with underlying heart disease, ventricular ectopic beats or non-sustained ventricular tachycardia raises the possibility of an arrhythmic origin of syncope. Documenting the correlation between symptoms and an arrhythmia through ECG monitoring is considered a gold-standard diagnosis of syncope. If syncope occurs during ECG monitoring with no symptom-ECG correlation, an arrhythmia can be excluded as a cause of syncope. Various methods of ECG monitoring are the following:

(i) **In-hospital telemetry monitoring** – This is indicated in high-risk clinical scenarios, and ECG features suggestive of life-threatening arrhythmia, as mentioned in Table 1.

(ii) **Conventional ambulatory Holter monitoring** – If a patient experiences syncope or near-syncope episodes greater than or equal to once per week, Holter monitoring is useful.

(iii) **External loop recorders** – If the symptom interval is less than four weeks, these devices can be considered. However, the technical aspect involved in the operation of these devices is a limiting factor.

(iv) **Implantable loop recorders (ILRs)** – ILRs require a minor surgical procedure and have a battery life of up to 36 months. Although an ILR has a high cost initially, if the symptom-ECG correlation can be attained, then the analysis of the cost-per-symptom-ECG yield has shown that ILRs are a more cost-effective strategy than the conventional strategy of investigation.\(^{17}\) In patients with unexplained syncope, use of an ILR for one year rendered diagnostic information in more than 90 percent of the patients.\(^{18}\) Therefore, ILRs are recommended in the evaluation of patients with recurrent syncope of unknown origin and in the absence of the high-risk features mentioned in Table 1. In the future, implantable monitor work-ups will be anticipated instead or before conventional work-ups.\(^{19}\)

(v) **Mobile cardiac outpatient telemetry systems** – These systems transmit ECG information over a wireless connection to a service center and then to a physician. Their role in the diagnostic work-up of syncope needs further study.

(vi) **Electrophysiological study** – an electrophysiological study (EPS) is useful when the initial evaluation indicates an arrhythmic etiology of syncope in ischemic heart disease. If a patient with a severely reduced left ventricular ejection fraction (LVEF) experienced syncope, we need not perform EPS as irrespective of the mechanism of syncope, an implantable cardioverter defibrillator (ICD) is indicated.\(^{20}\) An EPS is less useful for patients with non-ischemic dilated cardiomyopathy than for patients with a prior myocardial infarction.\(^{21}\) Generally speaking, the role of EPS in the work-up for syncope has decreased.

**Other cardiac investigations** – Echocardiography is helpful to diagnose structural heart disease and to risk-stratify patients with low ejection fraction. Exercise testing in the general population with syncope is only indicated if syncope occurs during or shortly after exertion and in patients with chest pain suggestive of coronary artery disease.
Neurologic evaluation – If a neurological basis of syncope is suspected, brain imaging with either CT or MRI is recommended.

Treatment
Syncope management essentially depends on the cause of the syncope that leads to the global cerebral hypoperfusion. It should focus on lengthening survival, limiting body injuries, improving quality of life, and preventing recurrences.

Reflex syncope – Non-pharmacological measures such as physical counterpressure maneuvers (PCMs), together with education and reassurance, are helpful in decreasing the recurrence of reflex syncope in patients who experience prodromal symptoms.22 Isometric PCMs of the legs (leg-crossing) or the arms (hand-gripping and arm-tensing) can increase BP during the imminent phase of reflex syncope, which helps to prevent or delay losing consciousness. In young patients with recurrent vasovagal symptoms, tilt training may be tried. However, this requires significant motivation, as it is comprised of prolonged periods of prescribed upright stances in order to reap the long-term benefit.23 Many medications have shown unsatisfactory results in the treatment of reflex syncope. Pharmacological therapy with midodrine may be suggested in addition to lifestyle measures and PCMs in these patients; however, it is limited by the necessity of frequent dosing.24 Prolonged treatment should not be advised for occasional symptoms. Betablockers have no role in the treatment of reflex syncope. Avoidance of a triggering event is the cornerstone treatment for situational syncope.

Orthostatic hypotension – The non-pharmacological measures mentioned above regarding reflex syncope can be considered for syncope due to OH as well. In the absence of hypertension, patients should be instructed to maintain adequate daily hydration (2 to 3 liters) and salt intake (10 grams).25 In patients with drug-induced autonomic nerve failure, the offending drug should be discontinued. Midodrine is more effective in these patient groups than in patients with reflex syncope. Fludrocortisone should be considered a supplemental therapy if required.26 Abdominal binders and/or compression stockings may be indicated in older patients to reduce gravitational venous pooling.27

Cardiogenic syncope – The treatment goals for cardiac arrhythmias and structural heart diseases as a cause of syncope are outlined as follows:28,29

1. Cardiac pacing is recommended in the following patients with syncope:
   - Cause of the syncope is established by symptom-ECG correlation to be due to sinus node dysfunction
   - Asymptomatic pauses greater than or equal to three seconds
   - Second-degree Mobitz, complete, or advanced atrioventricular block
   - Bundle branch block and positive EPS

2. Catheter ablation is the treatment of choice in both supraventricular tachycardia (SVT) and ventricular tachycardia (VT) in the absence of structural heart disease (except for atrial fibrillation) if the cause of the syncope is determined by symptom-arrhythmia correlation on the ECG.

3. Anti-arrhythmic drugs, along with rate-controlling agents, are recommended in patients with an onset of rapid atrial fibrillation as a cause of syncope. Drug therapy should also be considered in patients with SVT and VT presenting with syncope if catheter ablation cannot be attempted or has failed.

4. An ICD is recommended in the following patients with syncope.30 The main purpose of an ICD in these patients is to reduce the risk of SCD rather than preventing syncope recurrences.
   - Ischemic or non-ischemic cardiomyopathy with severely depressed LVEF or heart failure
   - Documented VT and structural heart disease
   - EPS-induced sustained monomorphic VT in patients with prior myocardial infarction.
   - In patients that are at high risk with hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy/dysplasia, Brugada syndrome and/or long QT syndrome.

Driving and Syncope
An important point to consider in patients with syncope is providing recommendations regarding automobile driving. Patients with syncope or aborted SCD believed to be due to temporary factors (such as acute myocardial infarction, bradyarrhythmias subsequently treated with pacing, drug effects, and electrolyte imbalances) should be strongly suggested after recovery not to drive for at least one month. Patients with symptomatic VT or aborted SCD, whether treated pharmacologically, with ICD, or with ablation therapy, should not drive for at least six months.31

Syncope Management Units
In spite of various published guidelines, the initial evaluation of a patient presenting with transient LOC varies widely among physicians and hospitals. This leads
to the inappropriate utilization of resources involved in syncope diagnosis and its management. Due to these implications, syncope management units were developed by creating standardized algorithms and assigning designated physicians who are experts in syncope management. The Evaluation of Guidelines in Syncope Study (EGSYS-2) utilized decision-making software based on European Society of Cardiology (ESC) guidelines along with the comprehensive assessment of syncope through a multidisciplinary approach. The results from this study showed a significant reduction in inappropriate hospitalizations, an improved diagnostic yield, shorter in-hospital stay, lower mean costs per patient and lower mean costs per diagnosis.32

Prognosis
The prognosis for a patient with syncope is mostly dependent on the severity of the underlying disease rather than the syncope event itself. Mortality was substantially worse in patients with structural heart disease as a cause of syncope. Reflex syncope generally carries with it a favorable prognosis.6 The risk of recurrence is highest among patients with cardiac syncope.9 The best predictor of recurrence with vasovagal syncope is the frequency of events in the preceding year.11

Summary
Despite progress in understanding the concepts of syncope, there is a significant gap in the application of this knowledge in clinical practice, which leads to unsatisfactory results. The presented new health care model, an introduction of syncope facilities and standardized guideline-based algorithms coupled with on-line decision-making software, needs further study. We hope these new methods in syncope management help to reduce inappropriate use of diagnostic tests and minimize excessive use of health care resources.

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About the Authors:
Mahheedhar Gedela, MD, Resident Physician, Department of Internal Medicine, University of South Dakota Sanford School of Medicine.
Kashif A. Shaikh, MD, Resident Physician, Department of Internal Medicine, University of South Dakota Sanford School of Medicine.
Naveen Rajpurohit, MD, Cardiology Fellow, Division of Cardiology, University of South Dakota Sanford School of Medicine.
Muhammad Omar, MD, Resident Physician, Department of Internal Medicine, University of South Dakota Sanford School of Medicine.
Scott Pham, MD, Sanford Heart Hospital, Sioux Falls, South Dakota; University of South Dakota Sanford School of Medicine.

Please note: Due to limited space, we are unable to list all references. You may contact South Dakota Medicine at 605.336.1965 for a complete listing.
Stop the Bleeding! Reversing the Effects of Direct-acting Oral Anticoagulants

By Janet Fischer, PharmD

In 2010, dabigatran, the first of the direct-acting oral anticoagulants (DOACs), was approved for the treatment of atrial fibrillation (AF) in the U.S. Since then, three additional DOACs have been approved – rivaroxaban, apixaban, and edoxaban – for the treatment of both venous thromboembolism (VTE) and AF. These agents have significantly expanded the options for long-term anticoagulation with the advantages of simplified dosing, rapid onset and offset, fewer drug interactions, and no laboratory monitoring compared to warfarin. One disadvantage of these agents, however, has been the lack of a reversal agent for instances of life-threatening bleeding. Warfarin has multiple reversal agents including vitamin K, fresh frozen plasma, and prothrombin complex concentrate that can be used in the event of bleeding. But up until recently, there have been no reliable options for reversal of DOACs.

The first reversal agent to receive Food and Drug Administration (FDA) approval was idarucizumab for the reversal of dabigatran. Dabigatran (Pradaxa) works by directly inhibiting both free and fibrin-bound thrombin, thus inhibiting clot formation.1 Idarucizumab is a humanized monoclonal antibody fragment that binds to dabigatran and its metabolites. Its affinity for dabigatran is much stronger than that of thrombin, resulting in rapid neutralization of dabigatran’s anticoagulant effect. The primary clinical trial supporting its efficacy was a prospective, multicenter, open label, cohort study of patients on dabigatran who had either uncontrollable or life-threatening bleeding, or who required surgery or an invasive procedure that could not be delayed for at least eight hours.2 An interim analysis of the first 90 patients was published in June 2015. Patients in the trial were treated with two intravenous bolus doses of idarucizumab (2.5 grams each for a total of 5 grams) given no more than 15 minutes apart. The effect of the reversal agent was monitored with two clotting tests to determine percent reversal of the anticoagulant effect, along with the clinical outcome of the patients. Idarucizumab provided 88 to 98 percent reversal of clotting effects within minutes of the first infusion and this persisted for 12 hours, dropping to 54 to 72 percent reversal at 24 hours. In addition, unbound dabigatran levels dropped to a level associated with no effective anticoagulation in 99 percent of patients within minutes of the first dose being given and remained that low in 79 percent of patients at 24 hours. Of 51 patients who had life-threatening bleeding, only 35 (69 percent) were able to be assessed for cessation of bleeding, which occurred at a median of 11.4 hours. Of 36 patients who underwent urgent surgery, normal intraoperative hemostasis was reported in 92 percent. There were 18 deaths, 10 related to the bleeding event and eight related to other conditions. One patient had a thrombotic event within 72 hours of receiving idarucizumab, and four others had thrombotic events seven to 26 days after treatment. None were receiving anticoagulation therapy at the time of their clot. The results of this trial were considered favorable compared to trials of prothrombin complex concentrate for warfarin reversal, though the trial was limited by the lack of a control group. The results of this interim evaluation led to the accelerated approval of idarucizumab by the FDA in November 2015, and it is available as Praxbind at a cost of $3,500 per treatment. The full study enrolled 513 patients and was completed in July 2016 but has not yet been published.

The release of Praxbind provides a treatment for life-threatening bleeding associated with DOAC use, but its specificity for dabigatran makes it ineffective for rivaroxaban, apixaban, and edoxaban, all of which work by direct inhibition of factor Xa. However, a factor Xa reversing agent has recently been developed and is undergoing clinical trials. Andexanet alfa is a modified recombinant DNA protein that was specifically designed as a reversal agent for factor Xa inhibitors.3 Andexanet acts as a factor Xa decoy, binding to rivaroxaban, apixaban, and edoxaban in vivo and displacing them from their site of action to restore factor Xa function. Its affinity for the drugs is about equal to that of native factor Xa. It has no intrinsic anticoagulant or procoagulant properties. In addition to reversing the DOACs that inhibit factor Xa, it is also expected to be effective in reversing parenteral factor Xa inhibitors such as low molecular weight heparins and fondaparinux. The first clinical trial of andexanet in bleeding patients was published in September 2016 and reported the results from the first 67 patients enrolled in the ongoing trial.4 It was designed as a prospective, open label, multicenter trial in patients who developed acute major bleeding within 18 hours of a dose of apixaban, rivaroxaban, edoxaban or full
dose enoxaparin. The drug was administered as a 15 to 30-minute intravenous bolus followed by a two-hour infusion. There were two different doses used depending on which factor Xa inhibitor the patient had taken and the time since the last dose. All 67 patients who received the drug were evaluated for safety, but the efficacy analysis only included 47 patients who were found to have baseline anti-factor Xa activity within or above the therapeutic range. The primary outcomes were percentage change in anti-factor Xa activity and the rate of “excellent or good” hemostasis 12 hours after the infusion. Of the 47 efficacy patients, 26 were receiving rivaroxaban, 20 were receiving apixaban, and one was receiving enoxaparin. The rivaroxaban patients had an 89 percent decrease in anti-factor Xa activity at the end of the bolus dose of andexanet and an 86 percent decrease at the end of the two-hour infusion. The apixaban patients had a 93 percent reduction at the end of the bolus with a 92 percent reduction at the end of the infusion. At four hours after the end of the infusion, the anti-factor Xa activity remained reduced by 30 to 39 percent in both groups. Thirty-seven of the 47 evaluable patients (79 percent) were judged to have excellent or good hemostasis at 12 hours. Thrombotic events occurred in 12 of the 67 patients (18 percent), with four occurring within 72 hours of the andexanet. Only one of the 12 had resumed anticoagulation before the thrombotic event occurred. No antibody production or infusion reactions were reported. The authors compared their results to the idarucizumab and prothrombin complex concentrate trials and felt that andexanet showed similar efficacy in reversing anticoagulation and restoring hemostasis, though once again, there was no control group. These results have been submitted to the FDA for drug approval. As of August 2016, the FDA has requested further information about manufacturing, as well as data to support inclusion of edoxaban and enoxaparin reversal in the product labeling. The trial continues to enroll patients with a goal of 250 total patients.

In summary, idarucizumab and andexanet alfa are two new anticoagulant binding agents that are effective in reversing dabigatran and the factor Xa inhibitors, respectively. Idarucizumab is given as two bolus doses and its effects last up to 24 hours, while andexanet requires a bolus and infusion, has two dosing strategies depending on which DOAC is being reversed, and its effects begin to wane at four hours after the infusion. They both have been shown to reverse the anticoagulant effects of their target DOACs within minutes of administration and improve hemostasis for up to 12 hours. It will be important for health care institutions to develop protocols to ensure judicious use of these expensive agents, as well as procedures to ensure rapid preparation and administration of the proper doses in the setting of DOAC-associated major bleeding. With proper use, it is expected that these agents will improve the safety of long-term anticoagulation for VTE and AF.

**REFERENCES**


**About the Author:**
Janet Fischer, PharmD, Professor of Pharmacy Practice, College of Pharmacy, South Dakota State University; Clinical Pharmacist, Sanford USD Medical Center.
Board News

By Margaret B. Hansen, PA-C, MPAS, Executive Director,
South Dakota Board of Medical and Osteopathic Examiners

The Board announces new and amended administrative rules affecting the practice of Medicine and Licensing

To view laws regarding your profession: visit the Board website and click on the Statutes and Rules tab on the right hand menu.

**Medicine**

- Opioid Prescriber Medical Documentation Rules ARSD 20:47:07:01 and 20:47:07:02
  - Provides standards as to what is necessary for medical record documentation for the treatment of chronic, non-cancer pain
  - Provides a definition of chronic pain
  - The South Dakota State Medical Association (SDSMA) provided input and recommendations

- Physician Assistant Supervision ARSD 20:52:01:03.01 and ARSD 20:52:01:03.02
  - Removes the requirement that a supervising physician must visit each PA practice location every 90 days
  - Eliminates the required in-person meeting as a condition of the supervision agreement
  - Allows the Physician/PA team to determine the best supervision arrangement

**Licensing**

- Genetic Counselors ARSD 20:82:04
  - Adds continuing education requirements for genetic counselors
    - 25 hours per year or maintaining national certification with either ABGC or ABMGG

- Board of Medical and Osteopathic Examiners ARSD 20:78:03, ARSD 20:78:04 and ARSD 20:78:05
  - Updates Board application, complaint, and contested case hearing procedures

- Medical Assistants ARSD 20:84
  - Updates definitions, application requirements, applicant qualifications, approval of medical assistant schools, and registration renewal requirements.
  - The Nursing and the Medical and Osteopathic Examiners Boards jointly regulate medical assistants
As medical professionals, you already know that tobacco use can be a tough habit to kick. And, it can be even harder for your postpartum patients.

About half of the women who quit smoking during pregnancy relapse in the first 6 months after delivery. That’s a big number and that’s why the South Dakota QuitLine is offering additional services to pregnant women enrolled in the QuitLine phone coaching program.

When your pregnant patients enroll in the QuitLine phone coaching program they will receive:

- **Individualized counseling** intended to help them quit and stay quit during this exciting and often stressful time
- **4 additional relapse prevention calls** which are an extension of the standard QuitLine phone coaching program services
- **Special incentives** – pregnant women who enroll in the program may be eligible for gift card incentives

Encourage your pregnant patients to enroll in the QuitLine phone coaching program by calling 1.866.SD-QUITS or better yet, fill out the Referral Form (SDQuitLine.com/providers) and fax it to us.

Together we can help pregnant & postpartum women quit & stay quit.
Positioned for the Future, Focused on Partnership

Empowering Consumers with Choice

DAKOTACARE’s exceptional distinction is its broad provider network. Patients can stay with their doctor, choose their hospital and go to the pharmacy of their choice.

~ E. Paul Amundson, MD, Chief Medical Officer for DAKOTACARE

Committed to Participating Providers

DAKOTACARE and the South Dakota State Medical Association have enjoyed a long history of cooperation and mutual trust over the years, with direct involvement of South Dakota Physicians. This is what sets DAKOTACARE apart.

~ Michael W. Pekas, MD, Associate Medical Director for DAKOTACARE

Focused on Quality Care and Outcomes

DAKOTACARE works in a collaborative, non-adversarial way with network physicians, placing a top priority upon helping providers make quality-based decisions in the best interest of their patients.

~ James A. Engelbrecht, MD, Associate Medical Director for DAKOTACARE

2600 W. 49th Street ~ Sioux Falls, SD
605.334.4000
www.dakotacare.com
Dear Participating Provider,

As a participating provider in the DAKOTACARE network, we value your partnership in delivering quality care to your patients.

On Monday, Aug. 22, DAKOTACARE received notice from Sanford Health that they would end their providers' participation in the DAKOTACARE provider network effective Jan. 1, 2017.

DAKOTACARE has a 30-year history of maintaining a broad network of providers, and we value the relationships DAKOTACARE has built with physicians. Avera had hoped to continue negotiations with Sanford and is still open to collaborating with them.

Our top priority is our DAKOTACARE members. We will communicate with our employer groups and insureds to help them understand how Sanford's decision impacts them.

For our members who are in certain active treatment plans with Sanford providers there will be provisions for continuity of care so they can conclude their care regimen. Our customer service representatives are available to assist you and any of your patients who may need to change providers in this transition as we approach the Jan. 1 effective date.

Our goal is to put patients first and find solutions to ensure DAKOTACARE groups and policyholders receive the access and coverage they need. Our commitment to our members and customers does not change.

We ask for your assistance and collaboration in transitioning patients, so they are impacted as little as possible and experience uninterrupted care.

Again, thank you for your partnership in providing quality care to the patients you serve. We will continue to communicate with you to keep you up to date with any new developments.

Sincerely,

E. Paul Amundson, MD
Chief Medical Officer
The early detection as well as the prevention of diabetes are crucial factors in the future of health care delivery in our country. This complex and chronic disease impacts families and communities as well as the patient. The Centers for Disease Control and Prevention (CDC) estimates that close to 10 percent of our population has diabetes with close to 26 percent of the population over 65 with the disease. Furthermore, close to 37 percent of adults 20 years or older have prediabetes with impaired fasting glucose or elevated hemoglobin A1C. It is the seventh leading cause of death and may be involved in contributing to some of the other causes. It is the leading cause of kidney failure, non-traumatic lower-limb amputation, and new cases of blindness in adults.

The 2016 Standards of the American Diabetes Association are a list for updated resources and guidelines. These include an expansion of screening recommendations. Also addressed are management of obesity, dyslipidemia, and hypertension in addition to glycemic control. Lifestyle therapy, previously known as modification, has its own section focusing on nutrition counseling and education. Physical activity, adequate rest, and behavioral support, including tobacco cessation, are also discussed.

In addition to the primary care provider, the Centers for Medicare and Medicaid Services (CMS), through agencies such as the Great Plains Quality Innovation Network (QIN), is hoping to expand community support systems to assist the patient in the multiple aspects of this disease. Social support systems, including education, concerning diabetes management may help those patients whose understanding or health literacy is limited. Management may be aided by these resources outside the provider’s office that promote a team approach to this disease. The burden of diabetes is higher in certain racial and ethnic groups due to multifactorial reasons. Tradition, culture, and food choice, as well as geographic location and socioeconomic status, may affect availability of treatment and diet options.

Screening can only be effective if action is undertaken to refer the patient for dietary counseling and exercise recommendations. This provides a baseline for further intervention with medication if and when needed. Glycemic control is crucial for management and complication prevention but has an important element of individual variance depending on patient age, comorbid disease, and exercise tolerance. Independent management and safety are the top priorities for any intervention. The cost of diabetes care from clinic visits to hospitalization to expensive medications can be a burden to many patients. Insurance coverage for this as well as diabetic supplies can be an enormous financial challenge but the cost of not controlling the disease is even higher.

One helpful option may be the utilization and collaboration with certified diabetic educators if and where they are available. They offer an opportunity for care improvement and patient family involvement. These are specialized health care providers who have the education, experience, and credentialing that is important in working with patients across the spectrum of the disease to better enable them to engage in impactful self-care.

This disease has multiple online resources, such as the guidelines mentioned above, that recognize organizations dedicated to making diabetic care affordable and accessible. One local example is the South Dakota Diabetes Coalition (www.sddiabetescoalition.org) which offers resources and membership for all those interested in diabetes in our state. The members include public and private groups who are committed to addressing this condition. In person meetings are held twice a year in Chamberlain allowing education and interaction for multiple types of providers and stakeholders. Presenters have included endocrinologists, dietitians, podiatrists, optometrists, and educators, as well as the Department of Health, patients, and special population groups.

The spectrum of diabetic care is broad, and though challenging, offers the opportunity to help patients understand their disease so they can play a role in its treatment. The management of this care requires a community-wide effort to assist in helping to diagnose and control this expanding problem.

If you are interested in learning more about these efforts, please feel free to contact us at: stephan.schroeder@area-a.hcqis.org, Denise Kolba at denise.kolba@area-a.hcqis.org, or Dawn Hahn at dawn.hahn@area-a.hcqis.org.
Early October, my belly started aching and over a week, with good local care, and after extensive testing, the diagnosis of cancer of the bile duct and pancreas came down upon me.

A large team of multi-specialists met and discussed my options, and they think I might have a chance at a surgical cure, but have recommended pre-surgery chemo-therapy, which has been started. When they go in surgically to remove the tumor, we will learn if it has spread or not.

So I am facing a formidable challenge, and as an experienced Internist, I probably understand this process more than almost anyone. I should add here that I have explored every option, including the Mayo and elsewhere, nutritional alternatives, everything. I am very comfortable with my recognized and experienced surgeon in Sioux Falls and his partner the oncologist. I also realize there is a significant chance that the tumor has spread, and long-term chemo may be my option.

A dear psychologist-minister friend from afar wrote and asked how my soul is with all this, and how should he pray for us. My answer was as follows:

“Dear Steve,

I was 16 when I faced the sudden accidental death of my older sister. Add to that, I’ve been a geriatrician for 38 years, and hospice director for more than 20, so you know I’ve been living with the reality of my own death for a long time. My faith surrounds and envelops me. I’m okay with dying. I am trying to put it off as long as I can, but I’m okay if it happens sooner.

I have had an absolutely great life, loved and played with gusto, gathered all the fun I could have at every juncture. I have done my level best to help people with the tools of my profession, and I even know that some days I made a difference. I’ve tried to be 100% honest at every turn. I’m surrounded by a wonderful spouse, and honest creative kids. I’m writing a book about health care at end-of-life. Our multi-faith choir sings hymns weekly to people in need. All that helps. Maybe I’m naive, but I sense my soul is content and even joyful.

If I die from pancreatic cancer at 67 or 68, my family will suffer some, but I know that in the long run, they will celebrate my life, and I would encourage that. My tombstone will allude to my oft’ repeated comment as we sail, even when there is no wind... "We’re not dead in the water." My tombstone shall read, "Finally, dead in the water." I love it... humor even unto death.

So, you asked how I want you to pray? I would ask you pray that all of us see and accept our own dying process. Pray that we learn to savor every moment, every friend, and every grandeur/smudge/scent/or splash of the world around us. And pray that we find a way to open our hearts to others, walk in another’s moccasins, and find compassion, even for our enemies.”

That is my prayer for all of you.
**For Your Benefit:**

**Shaping Your Profession**

The SDSMA has a member-driven focus on issues, programs and policies, professional involvement, personal development and representation in organized medicine.

- Leadership opportunities on SDSMA committees and task forces;
- Representation for students, residents, young physicians and senior physicians;
- Low-interest educational loans and scholarships for students and residents;
- Collaborating with the University of South Dakota Sanford School of Medicine on physician workforce and medical education funding;
- Networking with colleagues during SDSMA meetings, conferences, seminars and social events.

We want to help nurture your professional development and your personal development. If you have questions about these programs, give us a call at 605.336.1965, or visit our website at www.sdsm.org.

Thank you for your membership in SDSMA.

“For Your Benefit” is the SDSMA’s monthly update on programs and services available to physicians through their affiliation with the SDSMA.

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**New SDSMA Center for Physician Resources Series on MACRA**

The SDSMA Center for Physician Resources is excited to bring SDSMA members a new series on payment models!

The series kicks off at 7 p.m. CT Nov. 10 with the webinar,

**“MACRA: Paying for Quality.”**

This presentation will include information on the Quality Payment Program and HHS goals, MIPS, advanced APMs, participation incentives, and next steps.

To register for the webinar, visit www.sdsm.org.

Additional presentations in this series include:

**MACRA: Clinical Practice Improvement Activities**

Dec. 1, 2016

Additional information on the Quality Payment Program and MIPS, and clinical practice improvement activities performance category

**MACRA: Quality Performance Scoring**

Dec. 22, 2016

Key changes from PQRS, MIPS data submission options, and quality performance category scoring

**MACRA: Performance Categories and Scoring**

Jan. 12, 2016

MIPS payment adjustment, APM scoring standard, category scoring, CPS calculation, CPS comparison with CPS performance threshold, payment adjustment and scaling, and payment adjustment application

All presentations are at 7 p.m. CT and are free for SDSMA and SDMGMA members.

Source: SDSMA staff
2017 SDSMA Membership Dues Renewal Now Available

Annually, SDSMA members must renew their membership to continue receiving many great membership benefits. Membership renewal will take place on the SDSMA website at www.sdsm.org.

To ensure a smooth renewal process for 2017, complete the following today:

1. Log into your member profile at sdsm.org and enter your username and password. If assistance is needed, contact the SDSMA office at 605.336.1965 or membership@sdsm.org.
   a. Do not create a new account. All members have an account at sdsm.org.
2. Contact your office administrator to determine if you or your organization will be paying the dues so it’s clear who will be completing this online process.
3. Once you have logged into your account, proceed to the Pay My Dues link at the top of the page. Payment by electronic check and credit card are both accepted through your account. A receipt will be emailed to you upon completion of the payment.

For step-by-step instructions on how to renew visit the Membership tab at www.sdsm.org and select Renewal.

Those with questions may contact Laura Olson at 605.336.1965 or membership@sdsm.org.

Source: SDSMA staff

Legal Brief Highlight: Restrictive Covenants

South Dakota law generally restricts geographic and length of time provisions in employment agreements that prohibit former employees from competing with a former employer. Restrictive covenants are unethical if they are excessive in geographic scope or duration, or if they fail to make reasonable accommodation of patients’ choice of a physician.

The SDSMA has adopted the position of the AMA Council on Ethical and Judicial Affairs that restrictive covenants restrict competition, disrupt continuity of care, and potentially deprive the public of medical services, and because of those reasons, the SDSMA believes restrictive covenants should be discouraged in physician employment agreements.

For more information, download the SDSMA legal brief Restrictive Covenants at www.sdsm.org. Through the SDSMA Center for Physician Resources, the SDSMA has developed more than 50 legal briefs that are available to members. In addition, the Center develops and delivers programs for members in the area of practice management, leadership and health and wellness.

Source: SDSMA staff

Sign up to be Doctor of the Day at the State Capitol!

The SDSMA’s Doctor of the Day program is a huge success every legislative session.

During session, the SDSMA commits to providing a physician member to serve as Doctor of the Day for the State Legislature in Pierre. This volunteer commitment involves one day of service at the State Capitol by providing basic medical assistance to legislators and staff as needed.

As Doctor of the Day, you’ll have the unique opportunity to interact with legislators on the House and Senate floors and get a first-hand look at the legislative process and how it affects the practice of medicine. Your presence at the Capitol shows legislators not only your expertise but also your concern for the health of South Dakotans.

The SDSMA is in need of volunteers willing to spend a day to serve as Doctor of the Day. Each year we receive requests from physician assistants and advanced practice nurse practitioners who wish to participate in the program; it is critical that volunteer physicians are serving each day of session.

South Dakota’s 2017 Legislative Session opens on Jan. 10. For more information and to see a listing of available dates, visit www.sdsm.org. If you are interested in volunteering or have questions, please contact Mark East at 605.336.1965 or meast@sdsm.org.

Source: SDSMA staff
South Dakota Medicaid requires prior authorization for elective services received outside South Dakota. The South Dakota Department of Social Services (DSS) has provided the following information regarding out-of-state prior authorizations:

Requests for elective out-of-state services should be generated by the referring in-state physician/specialist at the time of the referral. Medical records from the visit that prompted the referral should accompany the prior authorization request form.

Requests from the out-of-state provider will only be accepted when a recipient’s care has already been established there. Requests from out-of-state providers should be accompanied by records of the recipient’s most recent services there.

Authorization requests should include a schedule of planned care throughout the next year if more than one service is anticipated. This will decrease the number and frequency of authorizations needed.

The division has up to 30 days to make a prior authorization determination. However, requests are generally completed earlier when sufficient documentation is received.

Prior authorization is only required for elective services. Any urgent or emergent care is exempt from prior authorization requirements. Retro authorizations can be requested after the service is provided if care was suspected to be urgent/emergent at the time, but will be billed as elective.

Visit the DSS website at dss.sd.gov/Medicaid to download the prior authorization request form and for a list of frequently asked questions.

Source: South Dakota DSS

“The Issue Is” is the SDSMA’s monthly update on key policy issues of importance to physicians.
CME Events

Continuing Medical Education events which are being held throughout the United States (Category 1 CME credit available as listed)

**November 2016**

- **November 3**
  Pediatric Grand Rounds: Pediatric Suicide
  AMA PRA Category 1 Credit(s)™ available
  Details and registration online: usdssom.learningexpressce.com

- **November 4**
  34th Annual North Central Heart Cardiac Symposium
  AMA PRA Category 1 Credit(s)™ available
  http://www.averu.org/health-care-professionals/continuing-education/

- **November 9**
  Internal Medicine Grand Rounds
  AMA PRA Category 1 Credit(s)™ available
  Details and registration online: usdssom.learningexpressce.com

- **November 16**
  Internal Medicine Grand Rounds
  AMA PRA Category 1 Credit(s)™ available
  Details and registration online: usdssom.learningexpressce.com

  VA Tumor Conference
  AMA PRA Category 1 Credit(s)™ available
  Details and registration online: usdssom.learningexpressce.com

- **November 30**
  Internal Medicine Grand Rounds
  AMA PRA Category 1 Credit(s)™ available
  Details and registration online: usdssom.learningexpressce.com

**December 2016**

- **December 1**
  Pediatric Grand Rounds
  AMA PRA Category 1 Credit(s)™ available
  Details and registration online: usdssom.learningexpressce.com

  VA Medical CME Activity: Advances in the Treatment of Hepatitis C
  AMA PRA Category 1 Credit(s)™ available
  Details and registration online: usdssom.learningexpressce.com

**DO YOU HAVE A CME EVENT COMING UP? WOULD YOU LIKE TO HAVE IT LISTED HERE?**

Contact: Elizabeth Reiss, South Dakota Medicine, 2600 W. 49th Street, Suite 200, Sioux Falls, SD 57105
Phone: 605.336.1965 • Fax: 605.274.3274
Email: ereiss@sdsmma.org

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The device, known as the Absorb™ stent from Abbott, is designed to open a blocked heart vessel, restore blood flow to the heart and then dissolve into the blood vessel over time. This temporary structure is made of a naturally dissolvable material commonly used in medical implants such as dissolving sutures.

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