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## Research

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# Cardiac Complaints Encountered After Use of Street Drugs: A Review of their Cardiac Toxicity Mechanism

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## ABSTRACT

**Objectives:** The upward trend leading to versatility in street drug (SD) usage paves the way to numerous complications to organ systems, including cardiovascular events. But, findings on cardiac complications, as well as their prevalence and survey from SD abusers are not encountered in the literature.

**Material and Methods:** In this survey study, patients admitted to the emergency department (ED) with suspected substance abuse were collected prospectively and cardiac complications were observed. The relationship between variables and all types of SDs were analyzed. Prevalence of the cardiovascular events were calculated. Also, uncommon cardiovascular events after SD use were defined.

**Results:** In a total of 425 (424 male, 98.4%) participants, cardiac complaints after substance use were noted in 14.6% (n=62). High degree AV-node conduction block secondary to synthetic cannabis, and moreover occlusive ST segment elevated myocardial infarction (STEMI) after cannabis use was identified. In other 2 cases, ecstasy use was associated with both STEMI and tachycardia.

**Conclusion:** Emergency physicians and cardiologist must be competent in the management of patients with substance abuse and potential novel cardiac complications. Especially young males with substance use and suspicious presentations such as syncope, palpitation, and vomiting complaints may be at risk. Cardiac complications on rhythm disturbance, conduction delay or obstructive myocardial infarct can become other than in literature.

**KEYWORDS:** Street drug; Marijuana abuse; Atrioventricular block; Unstable angina.

**ABBREVIATIONS:** SD: Street drug; ECG: Electrocardiogram; ACS: Acute coronary syndrome; ED: Emergency Department; STEMI: Segment elevated myocardial infarction.

## INTRODUCTION

Since street drug (SD) usage has become widespread, emergency department (ED) admissions of such cases and complications developing after substance use are observed with an increasing frequency.<sup>1-3</sup> Some of these are cases with severe cardiac complaints similar to the presentation of routine cardiac emergencies. However, some patients can hide the fact that they used a substance, which leads their underestimation as simple cardiac emergency cases without substance use. Moreover, development of cardiac problems associated with SD use is important since they may be of a type that is not commonly observed in literature. This research encountered cardiac complaints due to SD use for the 1<sup>st</sup> time or by addiction and in addition, important cases that were emerged different than in literature are defined.

**MATERIALS AND METHODS**

The study was reviewed and approved by local ethics committee. This prospective cross-sectional study was conducted in the ED of our tertiary-care hospital, between 1<sup>st</sup> January and 31<sup>st</sup> December, 2014. Written informed consent were obtained from the patient for publication of this study and accompanying images. Substance user patients over 18 years old diagnosed *via* self-reports or detected by the physician's queries were enrolled to the study. Cardiac complaints or accompanying other angina equivalent symptoms and their survey during the admission in the ED including electrocardiogram (ECG), blood gas analysis, blood biochemical parameters, Troponin I levels, consultations and cardiac intensive care unit admissions) were approached. Substance use characteristics are based on the personal statement of the patient, because of the tests for substance detection were not available. Patients were excluded from participation if they decline to give informed consent and disclaim using a SD. Statistical analysis was performed using SPSS for Windows, version 15.0 (SPSS Inc., Chicago, USA). Quantitative data are represented as ranges and mean±standard deviation. Types of SD consumed by the patients and their cardiac complaints, ECG findings, laboratory results were compared using Mann-Whitney U-test and Kruskal-Wallis significance tests were used for the comparison of dependent and independent variables. *p* values below 0.05 were considered statistically significant.

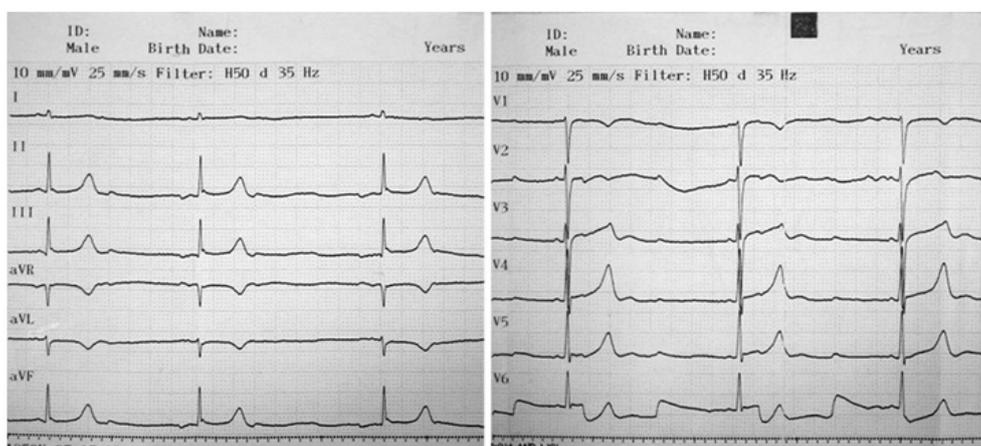
**RESULTS**

In a total of 425 cases, frequency of cardiac complaints observed after substance use was determined in 14.6% (n=62), and except for one, all of them were male. Distribution of these cardiac complaints were as follows: unconsciousness (more than a syncope attack) 10.4% (n=44), palpitation 1.9% (n=8, one case was first trimester pregnant), chest pain and accompanying other angina equivalent symptoms 1.9% (n=8, sweating, sense of fainting, vomiting, or abdominal pain), temporary syncope attack 0.2% (n=1), and stomach-ache with vomiting 0.2% (n=1) (Table 1). However, according to the complaint and ECG

evaluation, the rate of cases for which acute coronary syndrome (ACS) is considered and consulted with a cardiologist was found in 0.9% (n=4). Troponin I increase and/or cardiac arrest were not recorded in any of these cases. Statistical difference was not found between types of SD groups (marijuana, ecstasy, and amphetamine) consumed by patients cardiac complaints (unconsciousness, palpitation, chest pain, sweating, sense of fainting, vomiting, or abdominal pain), ECG findings (ST or T wave changes, tachycardia, bradycardia, non changes) and laboratory results (CK-MB and Troponin I) (*p*<0.05, *p*<0.05 and *p*<0.05 respectively). Here, in details of these important cases of SD users which were different than in literature.

**Case 1**

A 33-year-old 'bonsai' (a synthetic cannabinoid, including mostly JWH-018) abuser male patient was brought to the ED due to near syncope, sweating and vomiting after pure marijuana intake in the morning hours. He stated that he took only marijuana before arrival. High degree AV Block (Second degree AV/Mobitz type two Block) was observed on the electrocardiography trace (ECG; Figure 1). His initial vital signs were as follows; blood pressure 116/80 mmHg, heart rate 40 BPM, respiratory rate 12 BPM, oral temperature 98.6 °F, and a SpO<sub>2</sub> 100% on room air. Glasgow Coma Scale score was 15 and pupils were mildly dilated. His physical examination was unremarkable. No wall motion defect was found in transthoracic echocardiography and left ventricular ejection fraction was 60%. Normal sinus rhythm was restored following administration of atropine 0.5 mg intravenously. Cardiology consultation and admission to coronary intensive care unit was performed for monitoring the cardiac stability. Laboratory values of the patient were as creatine kinase (CK) 1792 U/I (normal range 0-171 U/I), CK-MB 9.01 ng/ml (normal range 0-5 ng/ml). No increase was observed in Troponin I level and in the repeated cardiac markers. Venous blood gas values were normal except for the lactate (2.1 mmol/L). Complete blood count revealed leukocytosis of 12.500 K/ $\mu$ L. It was learned that the patient left the hospital against medical advice during 1<sup>st</sup> day of admission in the coronary intensive care unit



ECG tracing demonstrates second degree type 2 (Mobitz type 2) block associated with cannabis use.

Figure 1: ECG trace from Case 1.

and had no complaints in the meantime.

### Case 2

A 19-year-old male admitted to the ED with the complaints of palpitations, chest pain and blurry vision after ecstasy (MDMA; 3,4-methylenedioxy-methamphetamine; also called yellow star, Bugatti, superman) use for the first time. He was completely healthy previously except for using unknown bodybuilder drugs (unknown substance; may be anabolic steroid or either SD). Vital signs on admission were as follows; blood pressure 118/80 mmHg, heart rate 132 BPM, respiratory rate 12 BPM, oral temperature of 98.6 °F and SpO<sub>2</sub> 100% on room air. His first ECG was evaluated as sinus tachycardia and benign early Repolarization. ST elevation (STE) in lead D1 and avL ≤1 mm emerged in the following ECG (Figure 2). Cardiology consultation was administered and 10 mg Isosorbide dinitrate was administered orally to the patient. Although STE was improved later, sinus tachycardia remained. The initial troponin I level in the ED was reported as <0.01 ng/mL (normal range 0-0.03 ng/mL), and CK-MB was 6.93 ng/mL (normal 0 to 7 ng/mL). Repeated measures after 4 hours revealed no increase in troponin I level and CK-MB was lowered to 5.92 ng/ml. Creatine Kinase (CK) levels were 679 and 577 U/L respectively. Acute coronary syndrome treatment protocol was started (Advertising Standards Authority (ASA), clopidogrel, enoxaparin), and he was admitted to the cardiology department with the pre-diagnosis of STEMI. A coronary stress test was primarily performed on the patient. Although the STE ensued during cardiac stress test, his cardiac catheterization revealed normal coronary arteries, no wall motion abnormalities, and normal systolic function.

### Case 3

A 31-year-old male patient admitted to the ED due to palpitations after use of ecstasy (MDMA) and alcoholic beverages in the previous evening. He had no chest pain. His vital signs were normal except rapid pulse rate (141 BPM) and venous blood

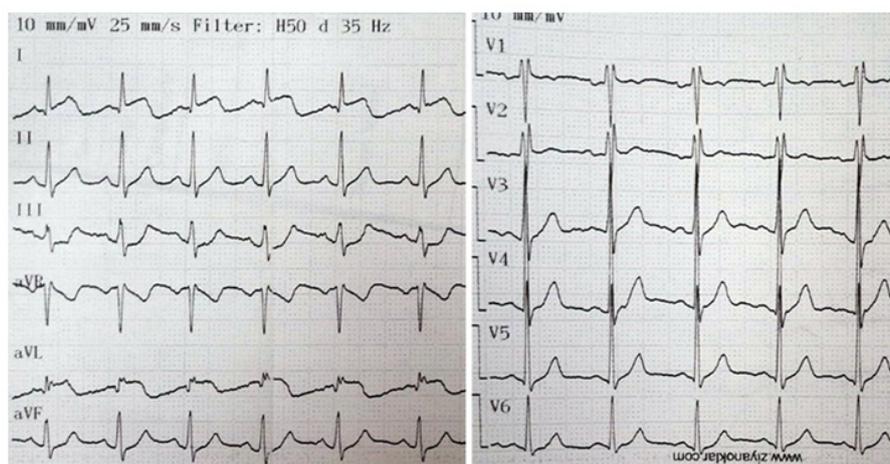
gas values were as follows; pH=7.6, pCO<sub>2</sub>=22.5 mmHg, lactate 4.2 mmol/L. Cardiac follow-up was performed as he had sinus tachycardia and STE ≤1 mm in lead V1 detected on ECG. After cardiology consultation, he was discharged due to restoration of normal sinus rhythm without antiarrhythmic administration and lack of any abnormality in the laboratory results.

### Case 4

A 44-year-old male admitted to the ED due to sudden-onset chest pain. Blood pressure was 155/112 mmHg, pulse rate 96 BPM and other vital signs were normal. The initial ECG revealed STE in the anterolateral leads. Coronary angiography was performed immediately. Endovascular stent was implanted after balloon dilatation to the patient whose left main coronary artery was observed as 100% occluded. No other complication was observed. It was learned that the patient confessed to cardiologists that he had been smoking for long years and he is a cannabinoid substance abuser. His pressure-like chest pain and cold sweating started two and a half hour after consumption of marijuana. His coronary angiography images are demonstrated in Figure 3.

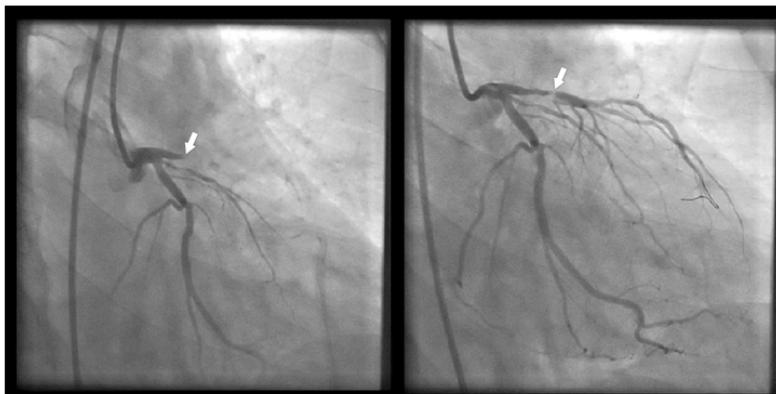
### DISCUSSION

The prevalence of usage of illegal substances, called SDs is 4-5.8% in world population.<sup>1</sup> Cannabinoid, synthetic cannabinoid derivatives, amphetamine or synthetic amphetamine derivatives are among the most commonly used SDs.<sup>1,3</sup> Marijuana is the most widely abused psychoactive SD that is obtained from jute plant *Cannabis sativa* ( $\Delta^9$ -tetrahydrocannabinol/ $\Delta^9$ -THC).<sup>1</sup> The variety in the street name of the cannabinoid can be confusing. The most frequently used street names of the cannabinoid widely vary according to the specific geographical region or location of the production origin: (*Marijuana, Cigarette, Crazy bud, Spice, K2, Sky, Saddam, Holland, Henry, Mary Jane, Bonsai, Jamaica, Bombay blue*).<sup>1,3</sup> Form of smoking the substance affects the onset and duration, and these characteristics are known



Leads D1 and avL showed STE following use of ecstasy in the patient with chest discomfort

Figure 2: ECG trace from Case 2.



Coronary angiography shows an occluded left anterior descending coronary artery. The patient had used cannabinoids before the chest discomfort and ECG findings indicated STEMI.

**Figure 3:** Coronary angiography slides from Case 4.

well by the users. The marijuana plant is generally dried, cut into small pieces and smoked by wrapping into a cigarette for a rapid influence (*joint effect*: it starts in 15 minutes and lasts for 4 hours).<sup>3</sup> Frequent side effects are dryness of the mouth, short-term loss of memory, hypo/hypertension, palpitation/tachycardia, nausea, vomiting and cardiac or cerebrovascular events.<sup>2-5</sup> Subjective increase in the perception, depersonalization, psychomotor coordination disorder, tremor, concentration loss, paranoia, schizophrenic symptoms may develop in addicts.<sup>5,6</sup> Prominent conjunctiva hyperemia appears in cannabis smokers.<sup>7</sup> Cannabis and their synthetics may be detected for weeks once it is taken into the body and is stated that making accumulation especially in the neurons and lipid membranes plays a role in addiction.<sup>5</sup> Cannabinoid receptors take place in the central neural and peripheral cells (CB1 and CB2 receptors, respectively).<sup>4,5</sup> It affects the amount of aminergic transmitters such as CB1 receptors with gamma aminobutyric acid and Glutamate. *Synthetic Cannabis* derivatives are sold in the markets as being 30-800 times more potent.<sup>1,2,4</sup> Synthetic derivatives that have a high central effect over CB2 receptors and that are commonly known include JWH-018 (*The most known street names are Jamaica, Bonsai, spice, K2, Holland e.g.*).<sup>1</sup> Users purchase the pure synthetic cannabinoid (i.e., JWH-018 powder) and extract and spray on any desired plant material.<sup>4</sup> There is no specific treatment for cannabinoid addiction, but it is recommended to evaluate the findings objectively and take symptomatic approaches.

Vascular side effects of cannabis and their synthetics are cardiac and cerebral.<sup>2,5,9</sup> Myocardial infarction has been previously reported in the setting of marijuana as well as synthetic cannabinoid use.<sup>4,10</sup> The proposed mechanisms for cardiovascular events due to marijuana use include an increase in catecholamines (released with the CB post receptor effects), carboxyhemoglobin levels, postural hypotension, increased cardiac workload, and an increase in oxygen demands with a decrease in myocardial oxygen supply.<sup>10</sup> In an article, that researched the effects from synthetic Cannabinoid, CB2 receptor knockout mice experiments suggested an association between CB2 receptor agonism and attenuation of post-myocardial infarction

ischemic-reperfusion injury.<sup>5,8</sup> Mobitz type 2 Block is observed as a different case according to the literature in the 1st case.<sup>9,10</sup> The rhythm responded to atropine. After marijuana use in the 4<sup>th</sup> case, angiography was performed by STEMI findings without troponin I increase and left anterior descending coronary artery was found to be 100% occluded: this is differently from vasospastic myocardial infarct that is expected in drug abusers. Cardiologist's reason for performing coronary angiography for a presumptive diagnosis of a STEMI, independent of the patient's marijuana use. Actually the cannabis user had a STEMI with completely occluded coronary artery (LAD). Literally, coronary vasospastic effect of the marijuana from the peripheral path and STEMI findings on ECG is called Type 2 myocardial infarction secondary to an ischemic imbalance.<sup>11</sup> Moreover, cannabis has a disturbing effect on coronary microcirculation and on coronary flow reduction.<sup>2,12</sup> Because the effects of cannabis cause catecholamine increase, this will lead to increase in heartbeat, increase of myocardial oxygen demand, direct response in the left ventricular function and sudden death. Additionally, it is thought that there is increased platelet coagulability.<sup>2</sup> Although, case 4 above had real coronary obstruction and STEMI on ECG, troponin increase did not occur.<sup>12</sup>

Acute exposure to MDMA/ecstasy has profound cardiovascular effects on blood pressure and heart rate in humans and animals.<sup>13</sup>

Serotonergic (5HT) tone will decrease in the myocardial wall as inversely proportional with ecstasy dosage. It was reported that after consumption of MDMA, carnitine increases in myocytes which leads to energy balance changes in the direction of increase in the fatty acid metabolism.<sup>13</sup> Likewise, it is observed that choline transmitter decreases and there are both parasympathetic desensitization and increased sympathetic effect in the tissue level. As in the 2<sup>nd</sup> and 3<sup>rd</sup> case presented, palpitations and accompanying STEMI on ECG can be encountered in ecstasy use. Coronary angiography was performed with coronary stress test positivity, but coronary blockage was not revealed. Similar case report is not frequent in the literature.

**LIMITATIONS**

The study was conducted as a single center study; hence, the results cannot necessarily be generalized to other EDs or other settings. Additionally, the same physicians performed all examinations within a year, also affecting the external validity. The advantage of this was, however, a consistent examination including cardiac procedures giving rise to collecting data about cardiac intensive care unit admissions of SD users. Blood or urine work-up was not performed to verify and characterize SD use, since resources were not available in the present hospital. Nonetheless, assessment of individuals using self-reports is cost-effective and is fairly accurate.

**CONCLUSION**

The frequency of cardiac complications by SD users is not high. However, emergency health care personnel must be on alert for young patients with substance abuse history, who present with altered mental status, chest pain and/or discomfort, syncope, palpitation and vomiting in terms of ACS. High-degree AV block and occlusive Type one STEMI may be observed after cannabinoid use.

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**CONFLICTS OF INTEREST**

The authors declare that they have no conflicts of interest.

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## Research

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# Sensitivity of Serum D-dimer for Spontaneous Subarachnoid Hemorrhage

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## ABSTRACT

**Study Objective:** Subarachnoid hemorrhage (SAH) activates the fibrinolytic system and increases serum D-dimer levels. These levels could prove diagnostically useful if reliably elevated in patients with SAH. Our goal was to calculate the sensitivity of serum D-dimer in detecting spontaneous subarachnoid hemorrhage.

**Methods:** We reviewed case records of all patients diagnosed with spontaneous SAH at our institution from 1990-2012. We excluded patients who had SAH from traumatic injuries, known intracranial pathology, as well as those having intracerebral hemorrhage. We recorded whether the D-dimer level was assessed in each patient, as well as the timing of the D-dimer measurement.

**Results:** We identified 368 patients who received a diagnosis of SAH, including 237 meeting inclusion criteria. One hundred eighty-five of these patients had a positive serum D-dimer after symptom onset, yielding a sensitivity of 78.1% (95% confidence interval (CI): 72.9-83.8%). Twenty-two patients had a serum D-dimer drawn within 12 hours of symptom onset, including 19 with positive D-dimer results, to yield a sensitivity of 86.4% (95% CI: 65.1-97.1).

**Conclusions:** Serum D-dimer levels exhibit high sensitivity among patients with spontaneous SAH. This finding warrants further investigation.

**KEY WORDS:** Subarachnoid hemorrhage; D-dimer; Spontaneous sensitivity.

**ABBREVIATIONS:** SAH: Subarachnoid hemorrhage; CFR: Case Fatality Rate; CT: Computerized Tomography; CSF: Cerebrospinal fluid; CTA: Chicago Transit Authority; MRI: Magnetic Resonance Imaging.

## INTRODUCTION

### Background

Headache accounts for 2% of Emergency Department (ED) visits, and subarachnoid hemorrhage (SAH) accounts for 1-3% of these headaches.<sup>1-5</sup> It is infrequent, yet deadly, with a case fatality rate (CFR) reported as high as 40-50%.<sup>2</sup> It can be difficult to diagnose, as neurologically intact patients presenting with only headache can account for half of all SAH at initial presentation.<sup>6</sup> The current diagnostic gold standard is high-resolution computerized tomography (CT) scanning, followed by lumbar puncture in patients with negative imaging.<sup>7</sup> The requirement for lumbar puncture is not ideal. It is often troublesome to patients, can be technically difficult and cumbersome, and can be fraught with complications including postural headache, nerve injury, epidural hematoma and both local tissue and CSF infections.<sup>1</sup> Furthermore, the cerebrospinal fluid (CSF) red-blood-cell (RBC) cut-off for the diagnosis remains unclear, and a traumatic puncture can lead to further uncertainty.<sup>8</sup> A more streamlined approach to quickly diagnosing SAH would be welcome.

### Importance

Serum D-dimer, a product of fibrin degradation, is physiologically activated in the acute stage

of SAH,<sup>9,10</sup> and is higher in patients with poor clinical outcomes after SAH, traumatic intracranial hemorrhage and intracerebral hemorrhage.<sup>10-16</sup> If the serum D-dimer level was reliably elevated in patients with SAH, it might provide a diagnostic alternative to lipoprotein (LP).

### Goals of this Investigation

In this study, we calculated the sensitivity of serum D-dimer in patients with spontaneous SAH, to determine if serum D-dimer could be an objective marker to help diagnose SAH.

## METHODS

### Study Design

We conducted a review of the medical records of human subjects. The project was reviewed and approved by the institutional human subjects review board.

### Study Setting and Population

All patients admitted to a large tertiary care hospital with a diagnosis of SAH (ICD-9, 430), between the years 1990-2012.

### Study Protocol

Our inclusion criteria were: age > 18, spontaneous SAH, and symptoms starting before serum was drawn. Patients were excluded if they had evidence of head trauma, subarachnoid blood from iatrogenic intervention, intracerebral hemorrhage, or concomitant intracranial pathology.

Our 2 formally trained data abstractors completed numerous "practice" abstractions prior to collecting data for the study. Periodic meetings were held with the abstractors to monitor progress and ensure uniform handling of the data. One-hundred-ninety charts were randomly selected to be reviewed by both abstractors to assess for inter-rater reliability. Both abstractors were aware of the purpose of the study. Disagreements between the 2 abstractors were resolved by a study author directly involved with the training of the abstractors.

### Methods and Measurements

Information abstracted included the patient age, sex, race, final diagnosis (including type of SAH), radiologist interpretation of all brain imaging (including CT, computed tomography angiography (CTA), and magnetic resonance imaging (MRI)), lumbar puncture results (if performed), time symptoms began, time serum D-dimer was collected and whether serum D-dimer was positive or negative. Patients that were "found down" were considered to have spontaneous SAH if no obvious trauma was seen on brain imaging.

For studies of deep venous thrombosis (DVT), a serum

D-dimer cut-off of 500 ng/ml has traditionally been used. It has been extrapolated for cerebral venous thrombosis (CVT) and aortic dissection.<sup>17-20</sup> The same cut-off was used in this study for serum D-dimer's that resulted after 2002.

### Analysis

We used Microsoft Excel (Office XP, Microsoft Corp, Redmond, WA, USA) to tabulate data and calculate the overall sensitivity of serum D-dimer for diagnosis of spontaneous SAH. This study was reviewed and approved by the Institutional Review Board (IRB) under expedited status. Informed consent was waived.

## RESULTS

### Characteristics of Study Subjects

We identified 368 patients who received a diagnosis of SAH during the study period. Two hundred and thirty-seven met inclusion criteria, and formed the final cohort. Our chart abstractors exhibited a kappa coefficient 0.75 in determining D-dimer outcome.

All but 4 patients were initially diagnosed *via* a non-contrast CT brain study. Two patients were diagnosed *via* lumbar puncture and 2 were diagnosed *via* MRI (Table 1).

### Main Results

One hundred eighty-five patients had a positive serum D-dimer after symptom onset, yielding a sensitivity of 78.1% [95% CI: 72.9-83.8%]. Twenty-two patients had a serum D-dimer drawn within 12 hours of symptom onset (Table 2). Nineteen had positive D-dimer results, yielding a sensitivity of 86.4% [95% CI: 65.1-97.1%]. All 22 patients in the 12-hour subset were diagnosed on the initial non-contrast CT brain scan.

### Limitations

This study has no table limitations. It is based on medical record review, therefore our conclusions are a reflection of the quality of the data in the patient records, and some data were not obtainable. For example, many patients did not have D-dimer levels assessed, and among those who did, the exact time of critical events such as symptom onset was frequently not recorded. Serum D-dimer testing is not mandatory at our institution, and its use in patients with SAH is arbitrary in terms of which patients underwent testing, and the timing of that testing. Most of these tests were ordered as part of a neurosurgical admission package at University of California, Los Angeles (UCLA) and were not prompted by specific presentations. Ideally, analysis of the serum D-dimer of numerous patients within the time frame of a typical ED visit would afford better understanding of the utility of this test in the setting of suspected spontaneous subarachnoid hemorrhage. Under the constraints of a retrospective chart analysis, few patients were identified with serum D-dimer levels

	All	Positive D-dimer	Negative D-dimer
<b>N (%)</b>	237	185 (78.1)	52 (21.9)
<b>Age- median (IQR)</b>	55.5 (45.3, 68.0)	58.0 (46.0, 71.0)	50.5 (43.5, 64.5)
<b>Sex (%)</b>			
<b>Male</b>	89 (37.5)	67 (36.2)	22 (42.3)
<b>Female</b>	148 (62.4)	118 (63.8)	30 (57.7)
<b>Race (%)</b>			
<b>Caucasian</b>	132 (55.7)	99 (53.5)	33 (63.5)
<b>African American</b>	15 (6.3)	13 (7.0)	2 (3.8)
<b>Asian/Pacific Islander</b>	37 (15.6)	32 (17.3)	5 (9.6)
<b>Unknown</b>	4 (1.7)	3 (1.6)	1 (1.9)
<b>Latino</b>	49 (20.7)	38 (20.5)	11 (21.2)
<b>SAH Type (%)</b>			
<b>Aneurysm</b>	160 (67.5)	129 (69.7)	32 (61.5)
<b>AVM</b>	30 (12.7)	21 (11.4)	9 (17.3)
<b>AVM and Aneurysm</b>	2 (0.8)	1 (0.5)	1 (1.9)
<b>Ependymal Bleed</b>	3 (1.3)	1 (0.5)	2 (3.8)
<b>Other/Unknown</b>	42 (17.7)	33 (17.8)	8 (15.4)
<b>How Diagnosed (%)</b>			
<b>CT non-contrast</b>	233 (98.3)	182 (98.4)	51 (98.1)
<b>CTA</b>	0 (0)	0 (0)	0 (0)
<b>LP</b>	2 (0.8)	2 (1.1)	0 (0.0)
<b>MRI</b>	2 (0.8)	1 (0.5)	1 (1.9)

Table 1: Patient demographic totals.

	All	Positive D-dimer	Negative D-dimer
<b>N (%)</b>	22	19 (86.4)	3 (13.6)
<b>Age: median (IQR)</b>	58.0 (46.0, 68.8)	58.0 (46.0, 66.5)	70.0 (50.0, 72.0)
<b>Sex (%)</b>			
<b>Male</b>	3 (13.6)	2 (10.5)	1 (33.3)
<b>Female</b>	19 (86.4)	17 (89.5)	2 (66.7)
<b>Race (%)</b>			
<b>Caucasian</b>	8 (36.4)	7 (36.8)	1 (33.3)
<b>African American</b>	2 (9.1)	2 (10.5)	0 (0.0)
<b>Asian/Pacific Islander</b>	4 (18.2)	2 (10.5)	2 (66.7)
<b>Unknown</b>	1 (4.5)	1 (5.3)	0 (0.0)
<b>Latino</b>	7 (31.8)	7 (36.8)	0 (0.0)
<b>SAH Type (%)</b>			
<b>Aneurysm</b>	21 (95.5)	18 (94.7)	3 (100.0)
<b>AVM</b>	1 (4.5)	1 (5.3)	0 (0.0)
<b>AVM and Aneurysm</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>Ependymal Bleed</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>Other/Unknown</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>How Diagnosed (%)</b>			
<b>CT non-contrast</b>	22 (100.0)	19 (100.0)	3 (100.0)
<b>CTA</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>LP</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>MRI</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>Minutes to D-dimer drawn: median (IQR)</b>	533 (351, 598)	437 (320, 620)	554 (544, 565)

Table 2: Patient demographics of 12 hr subset.

analyzed within the time of a typical ED visit resulting in clearly underpowered results. It is also possible that uniform testing under specified time constraints and with more enrolled patients would yield different outcomes. The study was conducted at single institution and is based on a small sample size, this therefore limits generalizability and robustness of our results.

The method of D-dimer measurement at our institution changed during the study. Patients enrolled from 1990-2001 had

a serum D-dimer that was a latex agglutination assay reported in ratios, producing an overall output of “*positive*” or “*negative*”. Patients enrolled from 2002-2012 had a mini VIDAS high sensitive D-dimer reported in ng/ml and fibrinogen equivalent units. While it is unclear the effect this had on the study, only 2 patients out of the 22 in the 12-hour subset had the outdated D-dimer test.

It is also worth noting that all of the patients in this study had a hemorrhage that was visible on high-resolution head

CT. In contrast, serum D-dimer levels are most likely to be useful in establishing a diagnosis in patients who have unremarkable head imaging results. It is unclear whether our results apply to patients with CT-negative SAH.

## DISCUSSION

To our knowledge, no previous study has examined the use of serum D-dimer as a diagnostic tool for assessing patients with spontaneous SAH. In this preliminary investigation, we found that serum D-dimer exhibited a sensitivity of 86.4% in detecting spontaneous SAH in the 1<sup>st</sup> 12 hours after symptom onset, a level of sensitivity similar to that of CSF xanthochromia.<sup>21</sup> While our findings are based on a very small set of patients, this observation naturally leads to the question of whether it would be possible to replace an analysis of CSF obtained by lumbar puncture (xanthochromia) with a measurement of a serum marker obtained on a peripheral blood draw (D-dimer). While patients are likely to embrace this option, the answer to this question will require further research and a larger population of test subjects. In particular, CSF analysis is not used in establishing the diagnosis of SAH in most patients, but is typically used to assess patients with unremarkable or non-diagnostic head CT results and small hemorrhages. If D-dimer measurements are to be clinically relevant, they too must retain high sensitivity among this same cohort. While high sensitivity is essential for establishing the routine use of D-dimer measurements, a lower sensitivity might still be acceptable in assessing patients who refuse lumbar puncture. It is also important to note that outside 12 hours, our observed sensitivity dropped to 78.1%. This is in agreement with previous studies showing that systemic coagulation and fibrinolytic system activation occurs after SAH.<sup>9-16</sup> The decrease in sensitivity with time may limit the utility of serum D-dimer assessment among patients with delayed presentations.

As newer CT scanner models develop improved sensitivity and a lower rate of false negatives in detecting SAH, there is increasing discussion over the utility of CSF analysis.<sup>22</sup> There is also evidence that obtaining CTA or magnetic resonance angiogram (MRA) can rule out aneurysm bleed with enough sensitivity to effectively make lumbar puncture obsolete.<sup>23</sup> Underfunded hospitals and those in third world countries, however, may rely on older model scanners unable to produce results with the sensitivity to rule out SAH without adjunctive testing. However, given the relative ease and affordability of measuring the serum D-dimer, further studies into the sensitivity of serum D-dimer in the detection of spontaneous SAH and its utility in the work up of these patients are warranted.

This study was a preliminary investigation, and our goal was to find a sensitive serum biomarker to aid in the diagnosis of SAH. Specificity of serum D-dimer for spontaneous SAH was not calculated. Specificity for DVT is strongly dependent on pre-test clinical probabilities and has been found to be as low as 35-54.7% given that elevated D-dimer are frequently found in hospitalized patients, the elderly, those with malignancy, trauma,

hemorrhage, recent surgery and cancer, among other causes.<sup>24-27</sup> It would likely be similarly poor for SAH.

Further studies with refined methodology and larger sample sizes are needed before serum D-dimer can be used in clinical practice for the detection of spontaneous SAH in our patients. If future studies reveal high sensitivities, serum D-dimer could be a viable modality to rule out SAH in patients with a negative CT brain scan, thus providing an alternative to lumbar puncture for low risk patients. This finding could be exceedingly helpful in the work up of patients with suspected SAH in underfunded or third world hospitals.

## CONCLUSIONS

In summary, serum D-dimer appears to be sensitive in detecting spontaneous SAH in our small patient population. Results from this study suggest a need for further investigations into its clinical use and potential incorporation into diagnostic algorithms for spontaneous SAH patients.

## CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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## Case Report

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# Ultrasonographic Diagnosis of Intussusception in the Emergency Department

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### ABSTRACT

Distinguishing life-threatening causes of vomiting and diarrhea in infants is challenging. The ability to quickly and accurately differentiate causes of the acute abdomen at the bedside without radiation exposure is an extremely valuable skill. Ultrasound is quickly becoming first line for many differentials of the acute abdomen including intussusception, appendicitis, and pyloric stenosis. Volvulus and mesenteric adenitis can also often be seen. This report details a case of pediatric intussusception diagnosed in the emergency department by emergency medicine clinicians. Additionally, we review the best technical approach to finding an intussusceptions using ultrasound. The sensitivity and specificity of ultrasound for intussusception approaches 100% with an experienced sonographer. Harnessing this skill has the potential to save a significant amount of time and lives.

**KEYWORDS:** Intussusception; Ileocolic; Vomiting; Diarrhea; Pediatric; Target; Bulls eye; Ultrasound.

### INTRODUCTION

Intussusception is the most common cause of pediatric small bowel obstruction. It occurs predominantly in 3 to 36 month old males<sup>1</sup> and the annual incidence is approximately 56 cases per 100,000 cases.<sup>2</sup> In contrast to adult intussusception, 2%-12% of intussusception cases in children contain a lead point such as Meckel's diverticulum.<sup>3</sup> "Currant jelly stools" are commonly misconceived to be a frequent finding. However, this late marker of bowel ischemia is found in only a minority of cases.<sup>3,4</sup> Since history is limited in nonverbal children, the burden of diagnosis relies on a careful physical exam and particular attention to overall appearance, lethargy or inconsolability of the infant. Even then, the classic presentation is not reliable, particularly in cases of small bowel obstruction.<sup>3</sup> computerized tomography (CT) and ultrasound (US) is diagnostic; however, ultrasound has the advantage of limiting radiation exposure. Availability of bedside point of care ultrasound (POCUS) to diagnose uncharacteristic cases of intussusception could prevent delay of diagnosis. Classically in the United States, ultrasound is performed by an ultrasound technician or radiologist.<sup>5</sup> It has not yet been widely adopted that a bedside point of care ultrasound (POCUS) by an emergency provider can replace a formal ultrasound by radiology if determined negative. However, studies indicate specificity of POCUS by emergency providers is approaching 100%.<sup>5</sup> Identification of an intussusception on POCUS could greatly impact the speed of disposition, particularly in departments without ultrasound and radiology available overnight. The diagnosis is made noting a "bulls eye" or "target" appearance<sup>6</sup> in transverse view, created by invagination of the intussusceptum (proximal bowel) into the intussusceptans (distal segment).<sup>2</sup> Early surgical intervention *versus* enema treatment is essential to limit morbidity and mortality.

**CASE REPORT**

A 13-month-old African-American male with a chief complaint of persistent vomiting for one day presented to the emergency department with his mother. The patient’s mother reported 9 episodes of vomiting that was associated with irritability and the patient’s pulling of his knees up to his chest. Vomiting was exacerbated with any feedings. His last fluid intake and wet diaper were the morning of presentation and both were decreased from baseline. The vomits was non-bloody, non-bilious, and not projectile. His last bowel movement was diarrhea without blood or melena and occurred the day before. There were no known sick contacts, recent travel, illness, fever, rash, prior conditions, medications, birth complications, or surgeries. The patient was fully immunized. No home therapies were attempted. Vital signs include a heart rate of 111, respiratory rate 20, blood pressure 94/51, mean arterial pressure 65, and his weight was 11.8 kg. On physical examination the patient was noted to be alert, non-toxic and in no acute distress. The abdomen was soft with slight

fullness to palpation of the right upper quadrant (RUQ) but no appreciable mass was palpated. The bowel sounds were normal and no organomegaly was noted. On palpation of the abdomen the infant cried, but otherwise the examination was normal. On rectal examination no bloody or melanotic stool was noted in the rectal vault, but the fecal occult test was positive. A radiograph of the abdomen revealed a paucity of cecal air. (Figure 1) Bed-side ultrasound images were obtained. (Figure 2)

**DISCUSSION AND CONCLUSIONS**

Even though the details of CT scan are superior,<sup>3</sup> ultrasound should be attempted initially for diagnosis. Sensitivity and specificity of ultrasound for intussusception approaches 100% with an experienced sonographer.<sup>3,7</sup> Accuracy of diagnosing an intussusception in the ED by a novice provider can be improved with didactic and focused training following the techniques for success outlined in Table 1.<sup>5</sup> Early intervention is key and is expedited by ultrasonographic diagnosis. The longer the bowel

**Figure 1:** Paucity of Air on Acute Abdominal Series.



**Figure 2:** Abdominal Ultrasound Demonstrating the Target or Bulls Eye Sign Characteristic of Intussusception.



**Table 1:** Techniques for Successful Ultrasound.

Techniques for Successful Ultrasound
1. Use a linear transducer (5-10 MHz)
2. Apply sufficient amount of ultrasound gel to easily sweep between locations
3. Start in the right lower quadrant, transverse orientation with the indicator pointed to the patient's right
4. Identify the psoas as your starting landmark
5. Adjust the depth appropriately
6. Sweep superiolaterally toward the gallbladder and liver landmarks
7. In the right upper quadrant, rotate 90 degrees clockwise (indicator toward patient's head)
8. Sweep across the epigastrium to the left upper quadrant in longitudinal orientation
9. Rotate the transducer counter clockwise 90 degrees in the left upper quadrant and sweep inferiorly to the left lower quadrant.

intussusception persists beyond 24 hours, the less chance that an air or contrast enema will successfully reduce it.<sup>2</sup> Surgical intervention should be considered early if the patient is unstable with suspected perforation or if enema treatment fails.<sup>2</sup>

#### CONFLICTS OF INTEREST

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# Unusual Rash Development in a 7-Year-Old Male

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### CHIEF COMPLAINT

Redness and swelling to left leg.

### HISTORY OF PRESENT ILLNESS

An otherwise healthy 7-year-old male presented to the emergency department complaining of a pruritic, red rash with that had increased in area over 7 days. The rash reportedly began as a localized lesion on his left lower extremity and developed a secondary diffuse rash over the trunk and upper extremities after the initial ED encounter. During the initial emergency department visit he was prescribed diphenhydramine and topical hydrocortisone with minimal relief. He denied any known environmental or allergen exposures or asthma history suggesting atopic dermatitis, or new exposures to medications. The patient and his parent also denied fever, lymphadenopathy, or any respiratory signs and symptoms. The leg lesion was not indurated or fluctuant to suggest underlying abscess. There were no other ill contacts or family history of similar rashes.

### PERTINENT PHYSICAL EXAMINATION

The patient was well appearing, well developed and well nourished with no acute distress. He had no signs of anaphylaxis with normal cardiac, lung, and abdominal exams. An eczematous erythematous fine maculopapular rash was limited to torso and extremities excluding mucous membranes, hands, feet, and groin as seen in the following images. The left lower extremity had a notable round 1 cm crusted plaque with excoriation on an erythematous base. Head, eyes, ears, neck, and throat (HEENT) exam was unremarkable without conjunctivitis, oral lesions, facial swelling, lymphadenopathy or erythema.

**Figure 1:** Primary Impetigo Lesion Partially Altered in Appearance due to the Recent Application of Topical Corticosteroids.



**Figure 2:** Diffuse Maculopapular Pruritic Rash, a Dermatological ID Reaction Manifestation.



**Figure 3:** Composite Image of the ID Reaction on the Extremity and Back as well as the Primary Lesion.



1. What is the condition?
2. What is the treatment of this condition?

#### ANSWERS

1. The rash on patient in this photograph represents a case of id Reaction. This is a type IV hypersensitivity reaction that results in a generalized, acute skin rash developing as a response to an underlying infectious agent or inflammatory skin condition.<sup>1-3</sup> In this case, the underlying cause is the impetigo found on the left lower extremity noted prior to the onset of the more generalized rash of the id reaction. Note the well-circumscribed erythematous border with central crusting on the image of the primary lesion. The appearance varies depending on the inciting source, but typically involves a symmetrical, maculopapular, pruritic rash distant from the inciting event site. No fungal or bacterial organisms are present outside of the primary rash site. The id reaction occurs 1-2 weeks after the initiating event, and severity increases with excoriation or inappropriate therapy.
2. The antihistamine and topical corticosteroid treatment previously prescribed to the patient are both indicated for symptomatic relief; however, eradicating the inciting source is the only way to rid the body of an id reaction. The time to resolution varies, depending on the underlying etiology. For this patient, mupirocin cream and oral cephalexin were necessary to clear the impetigo, allowing the id reaction to resolve subsequently. One should consider systemic corticosteroids for extensive, severe, or refractory cases. A dermatology consultation for follow-up is also warranted.

#### CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

#### CONSENT

Written informed consent was obtained from the patient who participated in this case.

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## Letter to the Editor

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# Non-Traumatic Dental Issues in Hospital Emergency Rooms: Solutions and Strategies

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## INTRODUCTION

Patients with dental pain have been increasingly accessing hospital emergency departments (EDs) to manage acute episodes of dental neglect.<sup>1</sup> These patients typically receive antibiotics and pain management medications in the ED,<sup>2</sup> but lack awareness of where and how to locate dental treatment offices or clinics to resolve the issue. This report focuses on innovative models that reduce ED costs, improve dental quality and bring community stakeholders together for the purpose of public benefit. Template steps are offered for those considering how to begin an ED referral program in their community.

While prevention programs may be numerous and accessible within a geographic area, patients frequently delay oral health services until there is an urgent need or may be unaware of service locations. Many health center dental departments report a 35-40%<sup>3</sup> missed appointment rate for adults with attempts at reducing barriers (transportation, health literacy and case management) to basic dental care.

As typical dental expenditures represent 2% of an overall state Medicaid budget,<sup>4</sup> it is that 2% which is frequently eliminated as state legislators respond to budgetary pressures. Comprehensive adult dental benefits (including preventive and restorative treatments) now exist in fewer than half of the U.S. states. The result of these cutbacks often leads to an increase in emergency room (ER) traffic for dental pain patients.<sup>5</sup>

There have been several studies and much discussion regarding hospital ED usage for patients suffering from dental pain. An estimated \$1.6 billion in healthcare costs<sup>6</sup> has been attributed to those who use hospital EDs as a first stop for urgent dental needs, despite Medicaid expansion.<sup>7</sup>

While insightful baseline data for such discussions has been somewhat limited by usual ED International Classification of Diseases (ICD) coding protocols, there are positive examples of innovation, which engage community partners to reduce unnecessary ED use by guiding patients into non-hospital settings, such as dental clinics or private offices.

While community health centers are mandated to provide emergency dental services, many dental departments within health centers are unaware of the volume of patients seen at the local hospital ED. Direct communication may be non-existent, with patients receiving a referral sheet in the ED listing a phone number to call for continuing care.

Models of ER referral offer template opportunities for replication in any location. These models are effective in reducing ED usage for dental pain which reduces costs and improves quality as patients are treated in appropriate settings.

**Program Example #1:** Community leaders met in the city of Muskegon, Michigan in 2009 to discuss steps to replicate the successful “Dentist’s Partnership” program, which began in

Battle Creek, Michigan (Calhoun County) in 2007. The Calhoun County program, with an annual budget of \$130,000, saw the combination of patients volunteering at nonprofit agencies in exchange for dental care reduce ED visits by 72% and generating a return on investment of 32.2% for every dollar invested over a six-year period.<sup>8</sup>

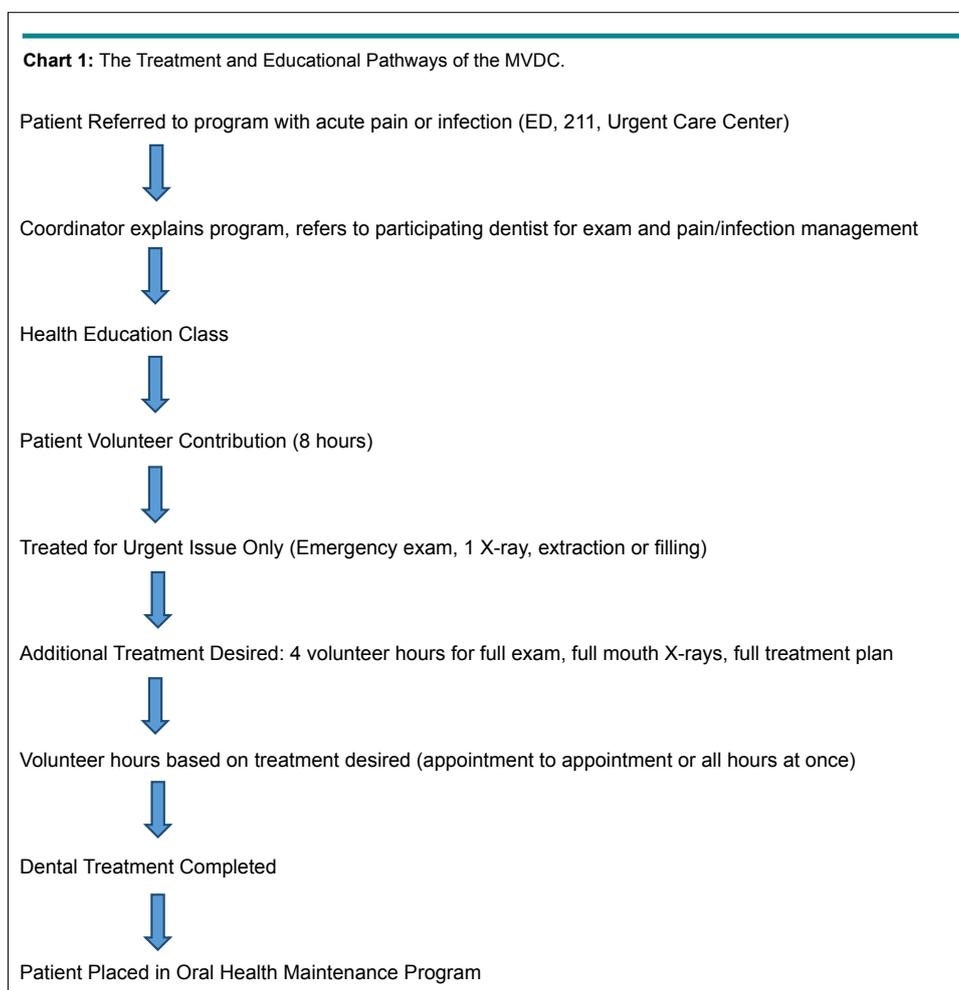
The Muskegon Community Health Project (MCHP) needs assessment revealed that unmet dental needs were a top priority for uninsured citizens. Beginning in 2014 with 10 dentists, grant donations of \$60,000 for a care coordination administrator with associated office equipment, over 70 patients were seen in the first year of the program.

By the conclusion of 2016, 21 dentists were participating in the program, over 290 patients were treated, who, in ex-

change for care, donated 10,806 hours of community service. The dollar amount of care rendered was \$270,150 and volunteer service was performed at 17 non-profit organizations. For every dollar invested in the Muskegon Volunteer for Dental Care (MVDC), the community sees over a \$3.00 return.

Several aspects of this program contribute to its success. Care coordination benefits both patients and dentists, who render care in their own offices. Dentists who choose to participate sign a letter of commitment to the program, as patients sign a letter acknowledging their responsibilities.

Each patient who participates in the MVDC program must attend an oral health education class and have individual oral health training, including tobacco cessation, with a dental hygienist who is their link to ongoing care (Chart 1) (Table 1).



**Table 1: Muskegon Volunteer for Dental Care ER Referral Program.**

	Annual ED non-traumatic dental visits	Financial impact	Patient Satisfaction and Volunteer Hours Provided
Before the program began (2012)	683	No dental treatment rendered No participating dentists	0% patient satisfaction No volunteer hours for non-profits
Outcomes (since 2012)	151	\$270,000 value delivered by 21 dentists	90% patient satisfaction 10,806 hours volunteered

**Program Example #2: Voucher or “Golden Ticket” Program**

This model resolves the acute ED visit, with the patient being referred for necessary care. The case management within this program is less than the previously discussed model (Example 1) and there is no patient volunteerism. The limited menu of services includes a dental exam, X ray, infection and pain management with an accompanying tooth extraction.

Two examples of this model are currently in operation. Since 2012, Catholic Charities Effingham, Illinois has been the “connector” between St. Anthony’s Memorial Hospital, and participating private dental offices. Catholic Charities contributes by supplying staff to work with adults 18 years of age and older to assist in managing dental emergencies with case management assistance. Participating dentists receive a flat fee per patient to cover necessary clinical procedures.

The program was developed after a community needs assessment, with access to dental care identified as a top priority. The hospital’s investment in the program was \$38,647 in FY 14/15 and \$32,214 in FY 15/16. Number of ED visits went from 135 patients in 1<sup>st</sup> Q FY 14/15 to 94 patients by 3<sup>rd</sup> Q FY 15/16.

Patients reported an improvement in overall quality of life and fewer work absences after receiving dental services. Additional options are being pursued for expanded treatment services and working with a local dental hygiene clinic for preventive services.

Another voucher ED Referral initiative is ongoing in Springfield, Missouri between two hospital EDs and a local Federally Qualified Health Center, Jordan Valley Community Health Center (JVCHC). This model began with a pilot program, which focused on patient integration into a dental environment in order to reduce inappropriate use of hospital EDs.

Mercy and CoxHealth Hospitals experienced 4,090 dental pain patients in their EDs, accounting for \$6.8 million dollars of costs in fiscal year 2014. Using care coordinators, the hospitals began faxing a voucher to JVCHC for every ED patient who presented with dental pain, with the patient being able to walk in during dental clinic hours for treatment.

This program was designed to offer patients quality access to dental care, an opportunity for continuing care within the health center and establishment of a dental home. This initiative was funded by the Missouri Foundation for Health and began in November of 2015. By July 30, 2016, a total of 1,801 patients have been referred (Chart 2).

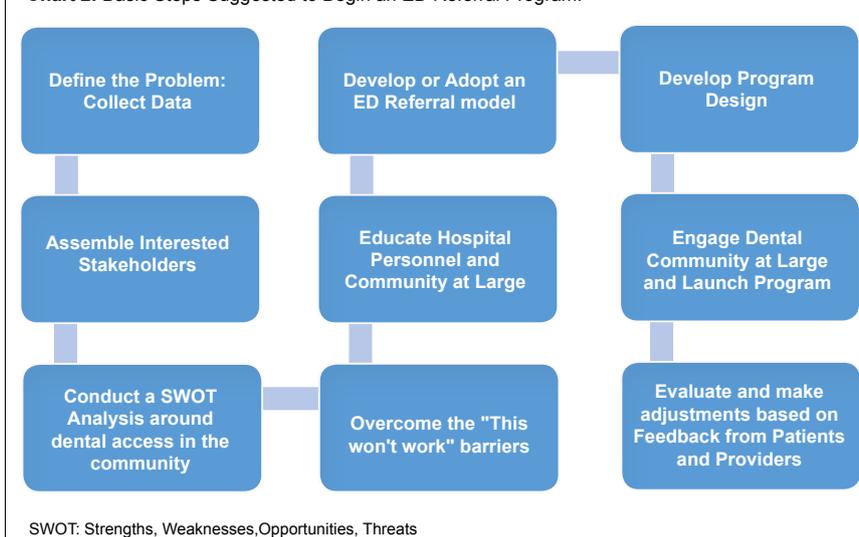
**CONCLUSION**

Models of ED Referral in the planning stage share several key steps in program development. These steps have proven successful in constructing programs which seek to connect care communities as hospitals often seek to partner with dental entities as a means to link oral health services to underserved patients who may have additional comorbidities.

Communication may begin with a health center dental director providing dental information to hospital staff and designing a triage document for ED physicians. Discussing health center dental department can be extremely valuable to hospital staff. Connecting a dental “face” with a name improves the comfort level of hospital staff making dental referrals.

Community efforts must be collective in designing an ED program. Oral surgeons, united way, hospital community outreach personnel, hospital nursing staff, service groups (Rotary, Kiwanis), teachers, school nurses, the community action agency, local small business groups and local foundations all can provide input into a community needs regarding oral health.

**Chart 2: Basic Steps Suggested to Begin an ED Referral Program.**



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