



## ARC SAC SCIENTIFIC REVIEW

### Aspirin for Chest Pain

#### **Question:**

Should the American Red Cross teach First Aid and CPR providers / rescuers to administer aspirin in the setting of chest pain suspected of being a heart attack?

#### **Overview:**

The incidence of heart attacks in the United States is one per 1000 population per year. Chest pain is a major manifestation of heart attacks. There has been popular press and advertising attention rendered to the common medical practice of administering aspirin in the setting of chest pain thought to be of cardiac origin. Thus it is very important that Red Cross First Aid personnel be advised on the implementation of this therapy which has been shown to be of benefit in the early response to heart attacks. Aspirin is a safe and effective treatment for heart attacks in combination with many other methods of care.

#### **Literature Search:**

A search of the literature was completed in 2001. The results of these studies were critically appraised for applicability to the question of efficacy and low complication rates for aspirin use. A second literature search was conducted of MEDLINE in 2006, using the keywords: aspirin and heart attack, myocardial infarction and stroke.

Several comprehensive reviews of the use of aspirin in cardiovascular disease along with scientific statements by the American Heart Association and the American Stroke Association were consulted.

#### *Triennial 2012 Literature Search*

The review of literature was limited to PubMed using the following parameters-

1. "Aspirin AND myocardial infarction AND mortality";
2. "Acute myocardial infarction AND aspirin";
3. "Aspirin AND acute myocardial infarction AND prehospital"; and
4. "Aspirin AND pre-hospital"

Inclusion criteria were limited to-

1. Human subjects
2. Randomized controlled trial, controlled clinical trial
3. Available abstract
4. Published in the English and published within the last 5 years. The last 3 or 5 years was selected to avoid overlapping with the 2010 American Heart Association and American Red Cross Guidelines for First Aid<sup>1</sup> and BLS guidelines.<sup>2</sup>

The initial search yielded-

1. 54 articles using the key terms "Aspirin AND myocardial infarction AND mortality."
2. One-hundred and fifty seven articles were identified using the key terms "Acute myocardial infarction AND aspirin."

3. Four were identified using the key terms “Aspirin AND acute myocardial infarction AND pre-hospital”
4. Three articles were identified using the key terms “Aspirin and pre-hospital.”

Of these articles-

1. 6 articles using the key terms “Aspirin AND myocardial infarction AND mortality.”
2. One-hundred and fifty seven articles were identified using the key terms “Acute myocardial infarction AND aspirin.”
3. Zero articles were identified using the key terms “Aspirin AND acute myocardial infarction AND pre-hospital”
4. Three articles were reviewed using the key terms “Aspirin and pre-hospital.”

In situations where an article referred a possible source, the abstract and/or article was located and reviewed at [www.pubmed.com](http://www.pubmed.com).

#### *Triennial 2015 Literature Search*

**(((chest pain) AND acute coronary syndrome)) AND ((aspirin OR ASA))) AND (((“first responder\*” OR “paramedic\*” OR “lay responder\*” OR “first aid provider\*” OR “Emergency Medical Services”[Mesh] OR “Emergency Responders”[Mesh]))) Filters:  
Randomized Controlled Trial retrieved 3 articles [below]  
[w/o RCT retrieved 39]**

Dracup 2009 - intervention vs. control group, population were patients at risk of CAD/ACS, mostly males age 67 >80% followed by a cardiologist  
Intervention was education on ACS symptoms, taking ASA, call 911  
Education increases the rate of ASA use, as well as time to 911; there were no differences in mortality  
NO significant side effects were reported

Fuchs 2010 - impact of providing 250 mg ASA IV on arrival at the ER - not related to our question

Bhattacharya 2010 - tirofiban for ACS - not appropriate for our question

**2 (“chest pain”) AND (“first responder\*” OR “paramedic\*” OR “lay responder\*” OR “first aid” OR “Emergency Medical Services”[Mesh] OR “Emergency Responders”[Mesh]) AND aspirin  
Filters: Humans; English**

**3 (undifferentiated) AND (“chest pain\*”) AND (“first responder\*”) OR “paramedic\*” OR “lay responder\*” OR “first aid” OR “Emergency Medical Services”[Mesh] OR “Emergency Responders”[Mesh])  
AND Humans[Mesh] AND English[lang] [w/o/aspirin]**

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Barron 2013 - A study of implementing a protocol, not the effects of ASA use, outcomes on survival - this study showed that EMDs can use a protocol and more patients get ASA - no data on safety, outcomes, etc.

Takakuwa 2010 - a review of the characteristics of patients with chest pain that got ASA in an ED, not a first aid perspective - not applicable

Colwell 2009 - review of an EMS systems adherence to a protocol for medics to give ASA to patients - not applicable

Whyte 2008 - financial motivators for medics to give ASA - not appropriate

**Martínez-Sellés 2008 - risk stratification with ECG and Troponin - not appropriate**

**Seferovic 2006 - tamponade, not ASA for ACS**

**Herlitz 2006 - a review of current treatments, not appropriate**

**Hooker 2006 - a review of why EMTs do not provide ASA - common is that a) the medics didn't believe it was ischemic pain and b) licence issues — this study shows that ECG and higher level risk stratification are needed to identify all cases of chest pain - and that basic symptoms may miss some presentations - no adverse reactions listed**

Meischke 2006 - education of seniors about the benefits of calling 911 for chest pain - not appropriate

McVane 2005 - review of paramedics use, and descriptions of why they didn't use ASA - 54% of ACS patients in this 2457 patient study got ASA. 79% of people who got nitroglycerin for ACS also got ASA [21% of patients who got nitroglycerin did not get ASA]. This shows that EMTs — and perhaps first aid providers — need more education on the benefit of ASA from outcomes vs. the use of NTG for symptoms [no outcome benefit] - interesting but no direct outcomes

Rittenberger 2005 - looked at reasons for delay of transport in EMS system - not directed related to ASA

Quan 2004 - a review of 25,600 ambulance cases, looking specifically for adverse events 0 none were found - ASA can be given safely out of hospital - helpful

Stoykova 2004 - results of a protocol for ambulance use of ASA - effect of implementing the protocol, not of the ASA

Snider 2004 - also a study of the results of a protocol implementation

Bledsoe 2003 - general review

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Woolard 2001 - benefits of audits in ambulance system to improve ASA use - not appropriate

Rothrock 2001 - gender inequality in ASA use - more commonly given to men vs. women by EMS systems

Herren 2001 - general review article

Brown 2000 - demographic factors affecting call 911 vs. delaying care - not appropriate

Weaver 1993 - prehospital fibrinolysis

Bland 1993 - prehospital fibrinolysis

**S1 ("paramedic\*" OR "lay responder\*" OR "first aid" OR "Emergency Personnel" OR "Emergency Responders" OR "lay public") AND (chest pain AND undifferentiated) AND Aspirin  
0 results**

**S2 ("paramedic\*" OR "lay responder\*" OR "first aid" OR "Emergency Personnel" OR "Emergency Responders" OR "lay public") AND chest pain AND Aspirin  
47 results chose 13 removing duplicates from Pubmed search**

**S3 (chest pain AND undifferentiated) AND Aspirin  
11 results**

**Selected 9**

Figgis 2010 - review of paramedics compliance - not applicable

Tataris 2015 - review of EMS use from database - effects of a protocol - not relevant

Woolard 2001 - review of paramedics adherence to a protocol

Yelaja 2001 - newspaper article

Ware 2012 - newspaper article

Elwood 2000 - ASA for prophylaxis in stroke, Alzheimers, ACS, and others - not appropriate

Osborne 2010 - newspaper article

Schlinkmann 2007 - newspaper article

Redd 2004 - ASA use within an hour of arrival in the ED improves survival vs. > 1 hours after arrival - reaffirms that early administration is better for ACS

*Triennial 2018 Literature Search*

**Search 1**

**Among adults experiencing chest pain due to suspected myocardial origin (P), does administration of aspirin (I), compared with no administration of aspirin (C), change cardiovascular mortality, complications, adverse effects, incidence of cardiac arrest, cardiac functional outcome, infarct size, hospital length of stay (O)?**

Search 1 PubMed

("chest pain") AND ("first responder\*" OR "paramedic\*" OR "lay responder\*" OR "first aid" OR "Emergency Medical Services"[Mesh] OR "Emergency Responders"[Mesh]) AND aspirin  
Filters: Humans; English and 2014-2017 3 results removing human did not change results

Search 2 PubMed

Search (undifferentiated AND "chest pain\*") AND ("first responder\*" OR "paramedic\*" OR "lay responder\*" OR "first aid provider\*" OR "Emergency Medical Services"[Mesh] OR "Emergency Responders"[Mesh])  
Filters: Publication date from 2014/01/01 to 2017/12/31; English  
12 hits

Search 3 Onesearch

( ("paramedic\*" OR "lay responder\*" OR "first aid" OR "Emergency Personnel" OR "Emergency Responders" OR "lay public") ) AND ( aspirin AND chest pain ) Limits: English, Publication date 2014 to 2017

9 four dups remov

PubMed, OVID - Medline, UI ONESEARCH  
English, dates 2014-2017

**20 results found**

20 articles excluded.

Reasons: no outcome data, epidemiologic data only, not relevant to topic.

**Hand search of references found 3 additional articles; 2 included, 1 excluded due to lack of relevance to the target population**

**Search 2:**

**Among adults receiving aspirin for chest pain due to suspected myocardial origin (P), does administration of enteric coated aspirin (I), compared with non-enteric coated aspirin (C), change time to systemic absorption, bioavailability, efficacy (O)?**

Search 1

((("Enteric coated" OR "enteric coating" OR ("Tablets, Enteric-Coated"[nm]))) AND (absorption OR disintegration OR dissolution OR resistance OR bioavailability) AND aspirin

Filters: Publication date from 2014/01/01 to 2017/12/31; English 13 hits

Search 2

((enteric coated OR non-enteric)) AND aspirin 54

Filters: Publication date from 2014/01/01 to 2017/12/31; English

adding in 'chest pain' to either search was 0 hits

Search 3

Search related "Journal of pharmaceutical sciences"[Jour] AND 100[volume] AND 9[issue] AND 3884[page] AND 2011[pdat] Filters: Publication date from 2014/01/01 to 2017/12/31; English 15 hits

Search 4

Search related "Basic & clinical pharmacology & toxicology"[Jour] AND 116[volume] AND 212[page] AND 2015[pdat] Filters: Publication date from 2014/01/01 to 2017/12/31; English 17 hits

99 hits = 73 after removing dups and not useful = 69

Same Search set run in IU OneSearch-multi-database  
only 4 unique hits - highlighted in olive

**73 total hits**

There were very few hits for adding in both chest pain and aspirin

PubMed, OVID - EBM Reviews (Cochrane DSR, ACP Journal Club, DARE), UI ONESEARCH  
2014-2017/Jul 18

English

73 articles reviewed, 73 excluded

Reasons: lack of clinical data, lack of pharmacokinetic data, not relevant to topic.

**Hand search of references found 2 additional articles; 1 included, 1 excluded due to lack of comparative data.**

**Three total articles included in new review.<sup>1,2,3</sup>**

**Scientific Foundation:**

Current literature supports the theory that unstable atherosclerotic plaques not only narrow vessels and retard blood flow but can rupture.

There is extensive evidence that aspirin has significant activity that interferes with the clotting actions of platelets. There is convincing data to support the use of aspirin to prevent myocardial occlusion and thus myocardial infarction both acutely and as a preventive measure. Studies have shown long-term aspirin therapy reduces the risk of coronary occlusive disease by as much as 25%. (1-3).

Aspirin has a rapid onset of action within 30 minutes. There is great therapeutic range and safety to aspirin use in the setting of acute ischemic chest pain patients. The risk of overdose is very low if two chewable baby aspirin tablets are stocked at a low level in personal first aid kits (two tablets, 81 mg each).

The acute coronary setting is accepted as being recognized if the lay rescuer notices that the patient displays:

- Chest pain or pressure (usually constant, heavy, squeezing)
- Shortness-of-Breath (air hunger, dyspnea)
- Sweating
- Weakness
- Radiation of unusual feelings or pain down the left arm or into the neck
- Nausea
- Fear of “impending doom”
- Change in the patient’s usual pattern of “Angina”

The "lay rescuer" should immediately call 9-1-1 or activate the local EMS unit; and make the patient as comfortable as possible.

If the patient is conscious and able to take oral medication and the patient denies

- Allergy to aspirin
- Stomach ulcer disease, or,
- Taking “blood thinners” (Coumadin, Warfarin, or other anti-platelet drugs)

the lay rescuer should offer two chewable (162 mg) baby aspirins or up to as much as one five grain (325 mg) adult aspirin tablet with a small amount of water.

If a patient has been revived or resuscitated from a suspected cardiac event, then the "lay rescuer" should offer aspirin treatment if the patient is able to ingest oral medications and does not have any of the above listed contraindications.

NOTE: Tylenol, Acetaminophen, Motrin, Advil, Ibuprofen and other pain killers are NOT equivalent to Aspirin. Combination and enteric-coated aspirin products are NOT supported by

this advisory because the literature does not contain studies of efficacy of these specific aspirin formulations in the acute chest pain setting.

*Updated Scientific Foundation from 2012 Triennial Review*

According the 2010 American Heart Association and American Red Cross Guidelines for First Aid it is difficult, even for the healthcare professional to differentiate patient experiencing chest discomfort of cardiac origin or from other chest discomfort.<sup>1</sup> Because of this it has been recommended that first aid providers assume that chest discomfort is cardiac in nature until proven otherwise. Cardiac chest discomfort is typically described as a “crushing” or “pressing” that is often accompanied by shortness of breath or perspiration. In some cases cardiac chest discomfort may not present with these classical characteristics, particularly in women. Thus standard of care requires immediate activation of EMS. It is recommended to not delay and not transport a patient yourself to a healthcare facility. While waiting for EMS to arrive, the “first aid provider may encourage the patient to chew 1 adult (not enteric coated) or 2 low-dose “baby” aspirin if the patient has no known allergy to aspirin or other contraindication to aspirin, such as evidence of a stroke or recent bleeding (Class IIa, LOE A).

Part 5 of the adult basic life support 2010 American Heart Association *Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care*<sup>2</sup> too stresses the importance in patient suffering from acute coronary syndrome (ACS) that Emergency Medical Dispatcher (EMD) and Emergency Medical Service providers must be trained to recognize ACS symptoms, even if atypical. They further states- “It is reasonable for dispatchers to advise patients with potential cardiac symptoms to chew an aspirin (160 to 325 mg), providing the patient has no history of aspirin allergy and no signs of active or recent gastrointestinal bleeding (Class IIa, LOE C).

*Updated Scientific Foundation from 2015 Triennial Review*

Review of 2015 ILCOR guidelines — references used were from 1979, 1988, 1990, 2001, 2002 and 2004 — no newer articles in their review either — ILCOR for public review indicate that ASA should be given for chest pain presumed to be cardiac in origin - the usual dose is 325 mg tablet, or 2-4 baby aspirin chewed

ASA remains useful for ACS [mortality benefit], although the ideal timing and appropriate undifferentiated population remains discussed. In patients with high probability of ACS or proven ACS, ASA is helpful. The risk for ASA in undifferentiated patients appears exceptionally low, but is not zero.

What is missing is an understanding of the patient populations that has a significantly high probability of benefiting from ASA administration, rather than just for people with ‘chest pain’. We recommend an ARC SAC FA review of signs, symptoms and risk factors of ACS that improves the sensitivity and specificity to the point that ASA benefit clearly outweighs the relatively low risk. On initial review, there are studies [eg Swap & Nagurney, JAMA Nov 23/30; 2005 - Vol 294, No 20, P2623] that will help inform on this.

*Updated Scientific Foundation from 2018 Triennial Review*



In 1979, Elwood and Williams<sup>1</sup> (LOE 1b) conducted a randomized controlled trial that evaluated the use of **aspirin on 28 day mortality** in patients with myocardial infarction. In this study researchers sent community practitioners who agreed to participate six sealed randomized envelopes containing either aspirin **300 mg or placebo**. Practitioners were instructed to give the intervention at first contact with a patient believed to have suffered a myocardial infarction. Follow up was completed by mail at one month with practitioners for subject details. The primary outcome was 28 day mortality. Infarction was determined as best judged by the practitioner. A total of 2530 subjects were enrolled, myocardial infarction was determined in 1705 patients who were used for analysis. There was no statistically significant difference in 28 day mortality in those treated with aspirin vs those treated with placebo (RR = 0.97; 95% CI 0.80-1.18). In those subjects who were treated within 4 hours of symptoms, again there was no difference in 28 day mortality in those treated with aspirin vs those treated with placebo (RR = 0.94; 95% CI 0.74-1.20). This study provided very low quality evidence, downgraded for bias, indirectness and imprecision. The authors concluded that this study provides no evidence that early aspirin intervention alters 28 day mortality in patients with myocardial infarction.

In 1990, Verheugt et al<sup>2</sup> (LOE 1b) conducted a randomized controlled trial that evaluated the use of early (onset < 12 hours) low dose aspirin (**100mg/day**) on infarct size and clinical outcome in 100 patients with anterior wall myocardial infarction. Patients were randomized to receive either **100mg** of plain aspirin or placebo per day. The initial dose was given within 12 hours of hospital admission along other treatments according to standard of care. Infarct size, as measured by cumulative serum lactate dehydrogenase (LDH), was the primary endpoint; death, re-infarction, unstable angina and revascularization were secondary endpoints. Three month follow up was completed in all patients. Early aspirin was not found to reduce the infarct size compared to placebo ( $1431 \pm 782$  U/L vs  $1592 \pm 1082$  U/L;  $p = 0.35$ ). Re-infarction occurred in one subject in the aspirin group versus six in the placebo group ( $p = 0.06$ ). This study provided low quality evidence downgraded for indirectness and imprecision. The authors of this study concluded that early intervention with low dose aspirin does not significantly influence infarct size, but does decrease the re-infarction rate.

In 2011 Sai et al<sup>3</sup> (LOE 1b) published a randomized crossover trial to evaluate the characteristics of **buffered aspirin tablets** and **enteric coated aspirin tablets** when **chewed** or **not chewed** on aspirin pharmacokinetics and platelet aggregation in healthy human volunteers. In this study 12 healthy subjects ingested either intact or chewed buffered aspirin (BA) or enteric coated aspirin (EC) tablets (Bufferin 81mg or Bayaspirin 100mg) and blood samples were collected at intervals after tablet ingestion for analysis. Volunteers participated in each stage of the trial with a 2 week washout period between stages. Two volunteers withdrew before completion of the study leaving only some of their data available for analysis. Mean residence time (MRT), which is defined as area under the first moment curve divided by area under the curve was a mean of 1.9 hours (SD = 0.9 hrs) for BA and 6.8 hrs (SD = 1.3 hrs) for EC. Chewing EC tablets shortened the MRT to 2.4 hrs (SD = 1.2 hrs). In this small sample size there was not a statistically significant difference between the MRT of intact or chewed BA versus chewed EC. Mean difference (MD): 0.05 hrs (95% CI = -0.4 – 1.4) for intact BA vs chewed EC; MD: 0.1 hrs (95% CI = -0.88 – 0.68) for chewed BA versus chewed EC. Intact and chewed BA as well as chewed EC inhibited platelet aggregation to a statistically significant degree by 20 minutes of ingestion, whereas it took unchewed EC 4 hours to attain this effect. This provided low quality evidence which was

downgraded for bias, indirectness and imprecision. The authors concluded that chewing EC aspirin greatly accelerated MRT and inhibition of platelet aggregation to a level comparable to that of intact and chewed buffered aspirin.

### **Recommendations and Summary of Triennial Review:**

The 2018 triennial review did not find significant updates to the 2015 review. With the 2017 search only three additional articles were found pertaining to the PICO. While all were randomized trials, they have significant limitations and evidence quality was downgraded. As summarized above, neither the Elwood nor Verheugt articles demonstrate a benefit in early aspirin administration in either infarct size or mortality. However both articles provide low quality evidence and have significant limitations. In addition, the Verheugt<sup>2</sup> article uses a smaller dose of aspirin than what is current recommended in both first aid recommendations and in clinical practice. For these reasons it was not felt that the evidence was not compelling enough to change the 2015 Treatment Recommendations. Sai et al<sup>3</sup> demonstrated that chewed buffered aspirin and enteric coated aspirin have a similar onset time of platelet inhibition. Although this is low quality evidence, it provides further data that chewed enteric coated aspirin tablets can be used as an alternative to chewed regular release aspirin tablets or chewable aspirin tablets if these options are not available to the provider.

Regarding the overall recommendations, there is little data to determine the risks and benefits of aspirin administration by first aid providers. For this reason, the recommendation for administration by first aid providers is less certain and, therefore, there are no Standards, only Guidelines. Based on the available evidence, it is felt that the majority of literature suggests that the benefit of aspirin administration outweighs the risks in those patients without known contraindications. Therefore, first aid providers may provide aspirin to patients suspected of having a heart attack and who have no known contraindications. However, due to the lack of definitive data, if the diagnosis is uncertain, the first aid provider may choose not to administer aspirin and wait for EMS arrival or presentation to the hospital. Literature demonstrates comparably fast onset times of chewed aspirin, whether it be regular release or enteric coated aspirin. Therefore, if aspirin is administered, it should be chewed. As prior literature suggests that the optimal dose of aspirin in a heart attack is between 162 mg and 325 mg, we included this in the recommendations. While these three articles do not provide information that would change current American Red Cross Treatment Recommendations, we felt that we should clarify some wording of the 2015 document. We clarified that “low dose” aspirin is 81 mg and that 2 to 4 of these tablets can be given. We also clarified that an “adult” aspirin tablet is 325 mg. Due to these minor changes this results in a recommendation of “revise”.

### **Treatment Recommendations - Revise**

Standards:

- None

Guidelines:

- It is reasonable for a first aid provider to provide ASA to a patient suspected of having a heart attack

- If there is uncertainty regarding the likelihood of a heart attack, it is reasonable to wait for the arrival of EMS
- The recommended dose of aspirin is 2 to 4 81 mg aspirin (162 -324 mg) or one 325 mg tablet (coated or non-enteric coated). The aspirin should be chewed.
  - Notes: Four, chewable, 81 mg tablets or one 325 mg non-enteric coated tablet should be included in First Aid Kits for use in the setting of acute chest pain.(FA KIT DOC)

Options

- None

**Algorithm for Aspirin Use by Lay Rescuers**

1. Evaluate patient for symptoms suggesting heart attack.
2. Call 911 or activate local EMS system.
3. Make patient as comfortable as possible.

**Is the patient conscious and able to swallow normally?**

No - DO NOT PROCEED WITH ASPIRIN THERAPY

Yes - Ask the patient the following questions:

**Do you have a known allergy to aspirin?**

Yes - DO NOT PROCEED WITH ASPIRIN THERAPY

**Has any physician ever told you not to take aspirin?**

Yes - DO NOT PROCEED WITH ASPIRIN THERAPY.

**Do you have any stomach ulcer disease or history of vomiting blood?**

Yes - DO NOT PROCEED WITH ASPIRIN THERAPY

**Do you take any blood thinners such as coumadin, warfarin or anti-platelet drugs?**

Yes - DO NOT PROCEED WITH ASPIRIN THERAPY

If the answer to ALL four questions is NO, the lay rescuer should offer two chewable (162 mg) baby aspirins or up to one five grain (325 mg.) adult aspirin tablet with water.

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