

# THE USE OF INTRAVENOUS IBUPROFEN IN POSTOPERATIVE PERIOD

Shirtaev B.K., Yerimova N.Z., Sundetov M.M., Khalykov K.U., Kurbanov D.R.,  
Akhbetova A.G., Akilbekov S.D., Mukashev S.E., Kanazov A.K., Bogdanova D.O.  
«A.N. Syzganov National Scientific Center for Surgery» JSC, Almaty, Kazakhstan

## Abstract

The article reflects the role of non-steroidal anti-inflammatory drugs in postoperative period. The study was conducted on the data of 94 operations of children aged from 10 months to 15 years (mean age 4.4 years). All patients of our center with esophagocoloplasty in the postoperative period received the drug «Intrafen» in injectable form, intravenously. Name of manufacturer of drug: GEN ILAC VE SAGLIK URUNLERI SANAYI VE TICARET, A.S. (Turkey). The main active substance of this drug is Ibuprofen 400mg/4ml for intravenous injection. Patients were injected intravenous ibuprofen at therapeutically effective doses for a minimal period of time. After receiving positive reactions to the drug at the initial stage of treatment, the dose and frequency of taking the drug was adjusted individually for each patient.

**Objective.** This work is dedicated to evaluate the role of the intravenous Ibuprofen in the postoperative period in surgical practice.

**Material and methods.** The study included 94 pediatric patients with esophagocoloplasty. Age of patients: from 10 months to 15 years (mean age 4.4 years), of which: 90 (96%) patients had post-burn stricture of the esophagus; 3 (3%) patients with esophageal atresia; 1 (1%) patient with a short esophagus. The number of female children - 51 (54.3%) patients, male - 43 (45.7%) patients.

**Results.** The total number of patients receiving intravenous Ibuprofen in the postoperative period was 94. The optimal dose showed a good therapeutic effect. At the optimal dosage of 20 mg/kg/day, two patients experienced intra-abdominal bleeding. Follow-up time: 2 weeks after esophagocoloplasty.

**Conclusion.** In patients with esophagocoloplasty, preventive intravenous administration of Ibuprofen showed a good therapeutic result. Patients noted a decrease in pain, which in turn led to a decrease in the need for emergency analgesia.

<https://doi.org/10.35805/BSK20221055>

Shirtaev B.K.  
orcid.org/0000-0002-0773-3878  
Yerimova N.Z.  
orcid.org/0000-0002-0565-5327  
Sundetov M.M.  
orcid.org/0000-0002-0387-5422  
Khalykov K.U.  
orcid.org/0000-0003-1266-697X  
Kurbanov D.R.  
orcid.org/0000-0002-0426-9387  
Akhbetova A.G.  
orcid.org/0000-0003-0122-3487  
Akilbekov S.D.  
orcid.org/0000-0003-4613-1658  
Mukashev S.E.  
orcid.org/0000-0003-3022-1093  
Kanazov A.K.  
orcid.org/0000-0002-6032-3085  
Bogdanova D.O.  
orcid.org/0000-0003-0398-5813

## Corresponding author:

Yerimova N.Zh. - MD, pediatrician,  
«A.N. Syzganov National Scientific  
Center for Surgery» JSC,  
Almaty, Kazakhstan  
E-mail address:  
nazier1611@gmail.com

## Conflict of interest

The authors declare that they  
have no conflicts of interest

## Keywords

intravenous ibuprofen, postoperative  
analgesia, pediatric esophagocoloplasty

## Отандан кейінгі кезеңде ибупрофенді көктамыр ішілік енгізу

Еримова Н.Ж., Ширтаев Б.К., Сундетов М.М., Халыков К.У., Курбанов Д.Р.,  
Ахбетова А.Г., Акильбеков С.Д., Мукашев С.Е., Каназов А.К., Богданова Д.О.  
«А.Н. Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ, Алматы қ.,  
Қазақстан

## Аңдатпа

Мақалада отадан кейінгі кезеңдегі стероидтық емес қабынуға қарсы заттардың рөлі айқындалған. Зерттеу 10 ай мен 15 жас аралығындағы (орта жас - 4,4) балаларда болған 94 отаның негізінде жүргізілді. Орталықтағы эзофагоколопластикасы бар барлық науқастар отадан кейінгі кезеңде «Интрафен» дәрілік затын инъекциялық формада, көктамыршілік жолмен қабылдаған. Бұл дәрілік затты өндіруші ұйымның атауы: GEN ILAC VE SAGLIK URUNLERI SANAYI VE TICARET, A.S. (Түркия). Дәрілік заттың негізгі белсенді құрамы көктамыр ішіне енгізуге арналған Ибупрофен 400мг/4мл болып табылады. Науқастарға көктамыршілік Ибупрофенді терапиялық эффе́ктивті мөлшерде аз уақыт кәлемінде тағайындадық. Емдеудің алғашқы сатысында-ақ дәрілік затқа оң жауап алғаннан кейін, дәрілік заттың мөлшері мен қабылдау жиілігі әр науқасқа жеке дара өзгертілді.

**Мақсаты.** Бұл жұмыстың мақсаты хирургиялық тәжірибеде отадан кейінгі кезеңдегі көктамыршілік Ибупрофеннің рөліне баға беру болып табылады.

**Материал және әдістер.** Зерттеуге эзофагоколопластикасы бар 94 педиатриялық науқас алынды. Науқастардың жасы: 10 айдан 15 жасқа дейін (орта жас - 4,4), соның ішінде: 90 (96%) науқаста – өңештің күйіктен кейінгі структурасы; 3 (3%) науқаста – өңеш атрезиясы; 1(1%) науқаста – қысқа өңеш. Әйел жынысты балалар саны – 51 (54,3%) науқас, ер жынысты – 43 (45,7%) науқас.

**Нәтижелер.** Отадан кейінгі кезеңде көктамыршілік Ибупрофен қабылдаған пациенттердің жалпы саны-94. Оңтайлы доза жақсы терапиялық әсер көрсетті. Оңтайлы дозада тәулігіне 20 мг/кг екі науқаста құрсақішілік қан кету байқалды. Бақылау мерзімі: эзофагоколопластикадан кейін 2 апта.

**Қорытынды.** Эзофагоколопластикасы бар науқастарда Ибупрофенді превентивті көктамыршілік енгізу жақсы терапиялық нәтиже берді. Науқастар ауырсыну сезімінің азайғанын байқады, ол өз кезегінде шұғыл ауырсынуды басуға деген қажеттілікті азайтты.

## Хат алысатын автор:

Еримова Н.Ж. – Дәрігер-педиатр,  
«А.Н. Сызғанов атындағы Ұлттық  
ғылыми хирургия орталығы» АҚ,  
Алматы қ., Қазақстан  
Электронды пошта:  
nazier1611@gmail.com

## Мүдделер қақтығысы

Авторлар мүдделер қақтығысы  
туралы мәлімдеме жасаған жоқ

## Түйін сөздер

көктамыршілік ибупрофен,  
отадан кейінгі анальгезия, балалар  
эзофагоколопластикасы

## Применение внутривенного ибупрофена в послеоперационном периоде

Автор для корреспонденции:  
Еримова Н.Ж. – Врач-педиатр, АО  
«Национальный научный центр  
хирургии им. А.Н. Сызганова»,  
г. Алматы, Казахстан  
Электронная почта:  
nazier1611@gmail.com

Конфликт интересов  
Авторы заявили об отсутствии  
конфликта интересов

Ключевые слова  
внутривенный ибупрофен,  
послеоперационная анальгезия,  
детская эзофагоколонпластика

Еримова Н.Ж., Ширтаев Б.К., Сундетов М.М., Халыков К.У., Курбанов Д.Р.,  
Ахбетова А.Г., Акильбеков С.Д., Мукашев С.Е., Каназов А.К., Богданова Д.О.  
АО «Национальный научный центр хирургии им. А.Н. Сызганова»,  
г. Алматы, Казахстан

### Аннотация

В статье отражена роль нестероидных противовоспалительных лекарственных средств в послеоперационном периоде. Исследование проводилось по данным 94 операции, у детей в возрасте от 10 месяцев до 15 лет (средний возраст 4,4 года). Все пациенты нашего центра с эзофагоколонпластикой в послеоперационном периоде получали препарат «Интрафен» в инъекционной форме, внутривенно. Наименование организации-производителя данного препарата: GEN ILAC VE SAGLIK URUNLERI SANAYI VE TICARET, A.S. (Турция). Главным активным веществом данного препарата является Ибупрофен 400мг/4мл для внутривенного введения. Пациентам внутривенный Ибупрофен ввели в терапевтически эффективных дозах в течение минимального периода времени. После получения положительных реакций на препарат на начальной стадии лечения, доза и частота приема препарата была скорректирована индивидуально для каждого пациента.

**Целью** данной работы является оценка роли внутривенного Ибупрофена в послеоперационном периоде в хирургической практике.

**Материал и методы.** В исследование включены 94 педиатрических пациентов с эзофагоколонпластикой. Возраст пациентов: от 10 месяцев до 15 лет (средний возраст 4,4 года), из них: у 90 (96%) пациентов - послеожоговая стриктура пищевода; 3 (3%) пациента с атрезией пищевода; 1(1%) пациент с коротким пищеводом. Количество детей женского пола – 51 (54,3%) больных, мужского пола – 43 (45,7%) больных.

**Результаты.** Общее количество пациентов, получавших внутривенный Ибупрофен в послеоперационном периоде – 94. Оптимальная доза показала хороший терапевтический эффект. При оптимальной дозировке 20 мг/кг/сутки у двоих пациентов было отмечено внутрибрюшное кровотечение. Сроки наблюдения: 2 недели после эзофагоколонпластики.

**Заключение.** У пациентов с эзофагоколонпластикой превентивное внутривенное введение Ибупрофена показал хороший терапевтический результат. Пациенты отметили уменьшение боли, это в свою очередь привело к снижению потребности в неотложной анальгезии.

## Introduction

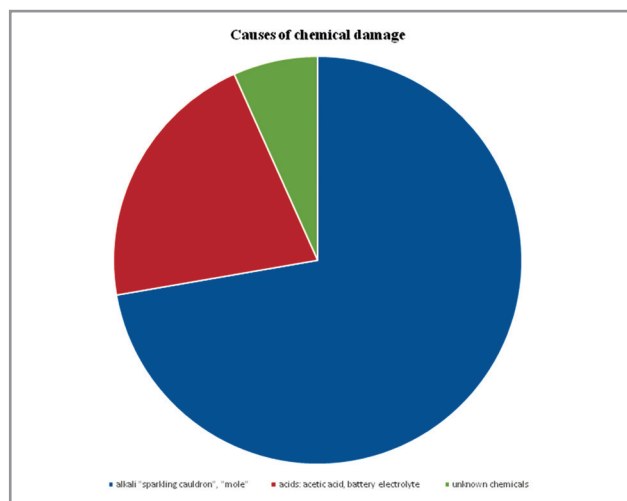
Causes of chemical damage: alkali “sparkling cauldron”, “mole” - in 65 (72.2%) patients; acids: acetic acid, battery electrolyte - in 19 (21%) patients and unknown chemicals - in 6 (6.7%) patient (Fig. 1).

At the moment, a hot topic in medicine is the treatment of acute postoperative pain. The main painkillers used in surgical practice are a group of analgesics based on opioid and non-steroidal anti-

inflammatory drugs (NSAIDs). Ibuprofen is most commonly used for children and is prescribed according to age and weight.

We used Ibuprofen solution for intravenous administration of 400 mg/4 ml for our patients. When used intravenously, the drug immediately enters the bloodstream. Ibuprofen is a non-selective, cyclooxygenase (COX) inhibitory NSAID that has anti-inflammatory, analgesic, and antipyretic properties.

Figure 1.  
Causes of chemical damage



The use of injectable forms of NSAIDs has an advantage in the speed of onset of the analgesic effect compared to taking standard tablets or capsules.

The use of several analgesics with different mechanisms of analgesic effect can help achieve the maximum level of pain relief when prescribing minimal therapeutic doses of several drugs that affect different levels of the nociceptive process. Thus, the analgesic effect of drugs increases, side effects decrease [1].

In patients in the postoperative period, the use of representatives of the NSAID group is pathogenetically justified, so we routinely prescribe them together with opioid analgesics. After extensive surgical interventions, the appointment of NSAIDs as basic analgesics can reduce the consumption of opioids by 20–60% [2].

For the treatment of pain syndromes with moderate to severe intensity, intravenous ibuprofen can be combined with intravenous opioid analgesics.

The use of NSAIDs helps to reduce the level of side effects inherent in «morphine-like» analgesics, such as paresis of the gastrointestinal tract, nausea, vomiting, sedation; improves the function of external respiration and pulmonary gas exchange, provides a quick awakening of the patient in the postoperative period. In the absence of the ability to take the last inside, we introduce them mainly intravenously in the form of a continuous infusion or bolus doses.

In multicenter studies, N. Moore et al. (1999) of the comparative efficacy and tolerability of first-line analgesics - acetylsalicylic acid, paracetamol and ibuprofen, used in 8677 patients, the authors demonstrate that the tolerability of the latter was comparable to that of paracetamol and was better than in cases of acetylsalicylic acid. Adverse events occurred more often in patients taking acetylsalicylic acid than in patients who were anesthetized with ibuprofen or paracetamol. The authors conclude that ibuprofen should be considered as the drug of choice in the practice of general practitioners in the short course, since there is a potential risk of developing a toxic effect when taking paracetamol. The most important advantage of ibuprofen over other NSAIDs is its high safety, proven by studies such as ARAMIS and PAIN [3].

Also, like most NSAIDs, ibuprofen is reversibly bound to plasma proteins (more than 99% at a concentration of 20 µg / ml). Protein binding is saturated, and at concentrations greater than 20 µg/ml, binding is non-linear. Dosage data for oral administration - the volume of distribution of ibuprofen varies according to age and temperature. In the human body, the release of ibuprofen is rapid and complete.

More than 90% of the absorbed dose is excreted in the urine as metabolites or their conjugates. Adequate use of intravenous ibuprofen at an adequate dose in patients with acute postoperative pain resulted in analgesia after the first dose and at the end of the course of analgesia in 90 children. It is advisable to prescribe intravenous ibuprofen within one week after surgery, every 12 hours at a rate of 20 mg / kg / day in case of pain syndrome of severe intensity or moderate intensity. The duration of intravenous drip should be at least 30 minutes. The highest recommended dose for children is 30 mg/kg/day.

NSAID use and risk of postoperative bleeding.

NSAIDs may have an antithrombotic effect and increase the risk of postoperative bleeding [4–8]. The possibility of this complication should always be considered when prescribing NSAIDs for patients undergoing surgery, even when it comes to outpatient interventions such as removal of the adenoids or tonsillectomy [9,10]. The frequency of bleeding from the area of the surgical wound in patients treated with NSAIDs exceeds 1%, but most of them are of low intensity and do not require repeated surgical intervention or blood transfusion. Risk factors are a large amount of surgical intervention, the presence of initial hemocoagulation disorders and the use of anticoagulants, which increases the risk of bleeding by 2-3 times [4,5].

All patients after esophagocoloplasty in the postoperative period received intravenous ibuprofen for one week. A single dose of ibuprofen for children is 5-10 mg/kg of the child's body weight 3-4 times a day. The maximum daily dose allowed in pediatric practice is 20-30 mg/kg of body weight. The duration of intravenous drip should be at least 30 minutes. We used a dosage of 20 mg/kg/day, every 12 hours. When using the above dosage, two patients received complications in the form of bleeding. Both patients had intra-abdominal bleeding, and therefore the drug was discontinued. Clinical, laboratory and instrumental research methods: In order to assess complications, postoperative bleeding in children, the results of a general blood test and coagulogram were used. Venous blood was used for the study. During the analysis of patient data, the following laboratory changes were obtained.

Patient M., 12 years old. Clinical diagnosis: Decompensated post-burn (means for cleaning cauldrons «sparkling cauldron», composition - alkali) cicatricial stenosis of the lower third of the esophagus. ICD disease code: K22.2. Obstruction of the esophagus (Table1, 2).

Component	Result	Comments	Normal values	Done at
Hemoglobin	66,0 g/L	Lowered	120-140	29.10.2018 14:45:09
Erythrocyte	3,14 10 <sup>12</sup> /L	Lowered	3,9-4,7	29.10.2018 14:45:09
Hematocrit	23,20 %	Lowered	35-47	29.10.2018 14:45:09

Table1.  
Hemogram. Patient M.

**Table 2.**  
Coagulogram. Patient M.

Component	Result	Comments	Normal values	Done at
Prothrombin time (sec)	11.1 s		11 - 21	29.10.2018 15:58:12
Prothrombinindex	70 %	<b>Lowered</b>	80,00 - 110,00	29.10.2018 15:58:12
INR	0,95		0,85 - 1,40	29.10.2018 15:58:12
Thrombintime	16,2 s		14,0 - 21,0	29.10.2018 15:58:12
APTT	23,30 s	<b>Lowered</b>	24,00 - 35,00	29.10.2018 15:58:12
Fibrinogen	4,50 g/L	<b>Raised</b>	2,00 - 4,00	29.10.2018 15:58:12

Patient L., 7 years old. Clinical diagnosis: Decompensated post-burn (liquid "mole", sewage cleaner, the main substance is sodium hydroxide) cicatricial stenosis of the middle third of the esophagus. The presence of a gastrostomy. ICD disease code: K22.2. Obstruction of the esophagus (Table 3,4).

**Table 3.**  
Hemogram.  
Patient L.

Component	Result	Comments	Normal values	Done at
Hemoglobin	69,0 g/L	<b>Lowered</b>	130-160	01.11.2021 6:57:47
Erythrocyte	2,54 10 <sup>12</sup> /L	<b>Lowered</b>	4,0-5,0	01.11.2021 6:57:47
Hematocrit	21,80 %	<b>Lowered</b>	39-50	01.11.2021 6:57:47

**Table 4.**  
Coagulogram.  
Patient L.

Component	Result	Comments	Normal values	Done at
Prothrombin time (sec)	won't clot		11 - 21	01.11.2021 6:27:51
Prothrombinindex	won'tclot		80,00 - 110,00	01.11.2021 6:27:51
INR	won'tclot		0,85 - 1,40	01.11.2021 6:27:51
Thrombintime	35,5 s	<b>Raised</b>	14,0 - 21,0	01.11.2021 6:27:51
APTT	36,70 s	<b>Raised</b>	24,00 - 35,00	01.11.2021 6:27:51
Fibrinogen	won'tclotg/L		2,00 - 4,00	01.11.2021 6:27:51

Main points regarding the development of complications associated with the use of NSAIDs.

All NSAIDs can cause complications in the gastrointestinal tract (GIT): dyspepsia, ulcers, bleeding and perforation of the upper and lower gastrointestinal tract, iron deficiency anemia (IDA) due to damage to the small intestine (NSAID enteropathy), cause exacerbation and complications of inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis (UC).

NSAIDs may increase the risk of bleeding after surgery and traumatic medical procedures.

The risk of complications can be significantly reduced with the use of drug prophylaxis. The main means of controlling the side effects of NSAIDs from the

upper gastrointestinal tract are proton pump inhibitors (PPIs) [11-14]. At present, there is no doubt about the ability of this class of gastroprotectors to reduce the incidence of ulcers, gastrointestinal bleeding and dyspepsia, significantly improving the subjective tolerance of NSAIDs. The use of a proton pump inhibitor prevents the risk of damage to the mucosa of the gastrointestinal tract, justified transfusion of blood components prevents the risk of developing metabolic disorders and blood clotting disorders.

The main preventive method of complications is the individual consideration of risk factors and the appointment of a more adequate dose of NSAIDs for each patient. Therefore, NSAIDs, including ibuprofen, should be used with caution in patients with gastric

ulcers or gastrointestinal bleeding. In patients with peptic ulcer and/or gastrointestinal bleeding, taking NSAIDs, the risk of developing gastrointestinal bleeding is higher than in patients without these diseases.

To reduce the risk of side effects associated with the gastrointestinal tract, the dose of NSAIDs should be reduced to the minimum effective dose as soon as possible.

In the event of gastrointestinal bleeding and ulcer formation in patients taking intravenous ibuprofen, treatment should be discontinued.

### Conclusion

Intravenous administration of ibuprofen in children was well tolerated for postoperative pain relief. The anti-inflammatory activity of intravenous ibuprofen helps prevent pain receptor sensitization and relieve tissue inflammation; stop the inflammatory cascade caused by invasive procedures. However, there are some safety concerns when using NSAIDs. Gastrointestinal and renal toxicity and the overall risk of bleeding are increased with the use of NSAIDs. However, many of these effects are associated with longer use. Intravenous ibuprofen is usually used on a short-term basis in hospitalized patients and in outpatient surgical procedures, which reduces the incidence of these problems.

We analyzed 94 studies using injectable ibuprofen, and all studies considered the efficacy of the optimal dose of intravenous ibuprofen in the postoperative period in children.

The present study showed that the preventive intravenous administration of ibuprofen led to a reduction in pain and a decrease in the need for emergency analgesia within one week after esophagocoloplasty in children.

### Practical recommendations:

1. Indications for the use of intravenous Ibuprofen are pain syndrome of various etiologies, including postoperative pain; treatment of pain syndromes of moderate and severe intensity, as an adjunct to intravenous opioid analgesics. The use of intravenous ibuprofen reduces the undesirable side effects inherent in "morphine-like" analgesics, such as toxic effects on the central nervous system, respiratory depression, paresis of the gastrointestinal tract.

2. It is advisable to prescribe intravenous ibuprofen for three days after surgery, every 12 hours at a rate of 20 mg/kg/day in case of severe or moderate pain. The duration of intravenous drip should be at least 30 minutes. The highest recommended dose for children is 30 mg/kg/day.

3. To reduce the risk of side effects associated with the gastrointestinal tract, the dose of NSAIDs should be reduced to the minimum effective dose as soon as possible.

4. In the event of gastrointestinal bleeding and ulcer formation in patients taking intravenous ibuprofen, treatment should be discontinued.

5. The specific antidote for Ibuprofen is not known. In case of overdose, symptomatic treatment is recommended.

### References

- Chrubasik S., Chrubasik J. Anesthesiology and Intensive Care/ [Anesteziologija i reanimatologija].-2000 - № 6– pp.48–52.
- Lebedeva R.N., Nikoda V.V. Pharmacotherapy of acute pain/[Farmakoterapija ostroj boli]. Air-Art., Moscow, 1998, p. 184.
- Moore N., E. Van Ganse, J-M. Le Parc. et al // Clinical Drug Investigation, – 1999 – Vol 18(2)– p. 88–98.
- Derry S., Moore R., Rabbie R. Topical NSAIDs for chronic musculoskeletal pain in adults. Cochrane Database Sys Rev., 2012, sep 12; 9 CD 007400
- Sostres C., Gargallo C., Lanás A. Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage. Arthritis Res Ther, 2013, 15 (suppl 3), S3
- Souter A. Controversies in the perioperative use of nonsteroidal anti-inflammatory drugs. Anesth Analg 1994; 79: 1178–1190
- Strom B., Berlin J., Kinman J., et al. Parenteral ketorolac and the risk of gastrointestinal and operative site bleeding. A postmarketing surveillance study. JAMA 1996; 275: 376–382
- Weber EW, Slappendel R, Durieux ME, et al. COX 2 selectivity of non-steroidal anti-inflammatory drugs and perioperative blood loss in hip surgery. A randomized comparison of indomethacin and meloxicam. Eur J Anaesthesiol. 2003 Dec;20(12):963-6.
- Bricker S., Savage M., Hanning C. Perioperative blood loss and non-steroidal anti-inflammatory drugs: an investigation using diclofenac in patients undergoing transurethral resection of the prostate. Eur J Anaesthesiol 1987; 4: 429–434.
- Wierod F., Frandsen N., Jacobsen J., et al. Risk of haemorrhage from transurethral prostatectomy in acetylsalicylic acid and NSAID-treated patients. Scand J Urol Nephrol 1998; 321: 20–22
- Nikanne E., Kokki H., Salo J., Linna T. Celecoxib and ketoprofen for pain management during tonsillectomy: a placebo-controlled clinical trial. Otolaryngol Head Neck Surg. 2005, 132, 287–294.
- Møiniche S., Rømsing J., Dahl J., Tramèr M. Nonsteroidal antiinflammatory drugs and the risk of operative site bleeding after tonsillectomy: A quantitative systematic review. Anesth Analg 2003; 96:68-77
- Kowalski ML, Asero R, Bavbek S, et al. Classification and practical approach to the diagnosis and management of hypersensitivity to nonsteroidal anti-inflammatory drugs. Allergy. 2013 Oct;68(10):1219-32. doi: 10.1111/all.12260. Epub 2013 Oct 5.
- White AA, Stevenson DD. Aspirin-exacerbated respiratory disease: update on pathogenesis and desensitization. Semin Respir Crit Care Med. 2012 Dec;33(6):588-94. doi: 10.1055/s-0032-1325618. Epub 2012 Oct 9.