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Understanding Pittaja Mutrakrichra: An Ayurvedic Perspective On Urinary Tract Infection

Dr. Adithya muraly v[1], Dr. Geetha B Markande[2] and Dr. Prashanth Jain[3]

[1]Final year PG Scholar (Dept. of *Roganidana Evum Vikriti Vigyan*), Alva's Ayurveda Medical College and Hospital, Moodubidire, Karnataka, India.

[2]Professor (Dept. of P.G Studies in Roganidana Evum Vikriti Vigyan), Alva's Ayurveda Medical College and Hospital, Moodubidire, Karnataka, India.

[3]Professor and HOD (Dept. of Roganidana Evum Vikriti Vigyan), Alva's Ayurveda Medical College and Hospital, Moodubidire, Karnataka, India.

Abstract: *Mutrakrichra* is a *Mutravaha Srotovikara* described in Ayurveda, characterized by difficulty and discomfort during micturition. Among its types, *Pittaja Mutrakrichra* presents with features such as *Sadaha*, *Krichramutrata*, *Muhurmuhurmutrapravruthi*, *Saruja*, and *Sapeetha Mutra*, closely resembling lower urinary tract infection described in modern medicine. This review analyzes the concept of *Pittaja Mutrakrichra* and correlates it with lower urinary tract infection. Relevant data were collected from classical Ayurvedic texts, contemporary medical literature, research articles, and authenticated online sources. Comparative analysis based on etiology, clinical features, pathogenesis, and disease course revealed a significant correlation between *Pittaja Mutrakrichra* and lower urinary tract infection. *Pitta-prakopaka* factors lead to alterations in urine characteristics and irritation of the *Mutravaha Srotas*, producing symptoms analogous to urinary tract infection. The study highlights the relevance of Ayurvedic principles in understanding urinary tract infection and supports their application in integrative preventive and therapeutic approaches.

Index Terms **-** *Pittaja Mutrakrichra*, *Mutrakrichra*, Urinary Tract Infection, *Mutravaha Srotas*

I. INTRODUCTION

Dosha, *Dhathu*, *Mala* are the basic supportive pillars of the *shareera*[1]. *Mutra* being one among the *Trimala* does *kledavahana*[2]. The list of the *Adharaneeyavega* comprises *Mutravegadharana* too[3]. Disorders related to *Mutra* have been elaborately explained by our *Acharyas* and *Mutrakrichra* is one among them *Pittaja mutrakrichra*- a mootravahasrotovikara is characterized by *krichatha* of *mutra*, *muhurmuhurpravruthi*, *sarakta*, *sadaha*,*saruja*, *peetamutrapravruthi*[4] which mimics Urinary Tract Infection. In general practice, UTI amounts for 1-3% of the consultation and 50% of women suffer from UTI[5].

II. AIMS & OBJECTIVES

Critically analyse the concept of *Pittaja Mutrakrichra* by comparing with lower urinary tract infection.

III. MATERIALS & METHODS

All relevant evidence related to *Mutrakrichra* and lower urinary tract infection was gathered from classical Ayurvedic texts, contemporary literature, relevant research articles, and authenticated internet sources. The concept of *Pittaja Mutrakrichra* was analyzed and correlated with lower urinary tract infection

NIDANA[6]

Acharya Charaka described the etiology of *Mutrakrichra* in the *Trimarmeeya Adyaya* while discussing the diseases of the *Basti*, whereas *Acharya Sushruta* and *Vagbhata* did not provide separate mention of the etiological factors.

Excessive consumption of *Rooksha Ahara, Madya, Adyashana, Ajeerna Bojana*, and an overindulgence in *katu, Amla*, and *Lavana* are considered *Aharaja Nidanas*. *Viharaja Nidanas* include *Ativyayama, Drutaprustayana, Vegadharana, and Atistree sevana*.

Anya karanaja Nidanas are *Teekshnoushada Sevana* and *Poorvajanma krita Papa*.

Table No. 1: Nidanas of Mutrakrichra according to different authors

Sl. No.	Aharaja Nidana	Ca[7]	Mn[8]	Bp[9]	Yr[10]
1.	*Rooksha ahara*	+	+	+	+
2.	*Madya sevana*	+	+	+	+
3.	*Anupa mamsa sevana*	+	+	+	+
4.	*Matsya sevana*	+	+	+	+
5.	*Adhyashana*	+	+	+	+
6.	*Ajeerna bhojana*	+	+	+	+
	Viharaja Nidana				
1.	*Vyayama*	+	+	+	+
2.	*Nithyadruta Prastayana*	+	+	+	+
	Anya Karana				
1.	*Teekshna Oushada*	+	+	+	+

Vata get vitiated due to intake of *Rookshahara*, which possess *Rooksha Guna*. As a result, is reduction of urine output and drying of body fluids due to *Shoshana Karma* of this *Rooksha Guna*. *Acharya Hareeta* explained that excess intake of *Katu-Amla-Lavana Ahara* leads to *Pitta Prakopa*, which makes the urine concentrated, exhibiting bad smell which favours the growth of microorganism. *Kapha Dosha* can be vitiated by intake *Anoopamamsa-Anoopamatsya* leads to delayed production of urine and prolonged retention of urine in the Basti. The *Ushna-Theekshna-Rooksha- Ashukari Guna* of *Madya* vitiates *Vata* & *Pitta* and it also possess *Amla Vipaka*. So *Atimadyasevana* result in change in urine ph. *Atistree Sevana* is considered one of the direct causes of bacterial infections in married couples, particularly in women, due to their anatomical structure. *Nityadrutaprustayana* leads to *Vata Prakopa* especially *Apana Vata Dusti, Kha Vaigunya* and *Vegadharana*. Administering *Teekshna Aushadha* results in *Shoshana* of *Dravadhathu* leading to increased

concentration of urine[11]. Due to these *Dosha Prakopaka Nidana*, results in vitiation of respective *Doshas* which gets lodged in *Mutramarga* by *Khavaigunya* and produces *Dosha Dooshya Samurchana*, leading to an increase in urine concentration, a change in pH, urine retention, and suppression of urination.

PURVA ROOPA

Purvarupa is not specifically mentioned in *Pittaja Mutrakricchra*, but according to *Chakrapani's* commentary on (Ca.Sa.Ci.11/12), *Lakshana*s of the *Vyadhi* that are expressed in a milder or incomplete form are to be considered as Purvarupa. Considering this, we can state that the *Purvarupa* is to be seen as the many *Lakshanas* of *Mutrakricchra* when they are presented in a milder form. The onset of the urinary tract infection is acute. The inability to detect *Purvaroopa* at this early stage can be explained. The illness appears early or progresses to *Vyaktavasta*, the next stage of *kriyakala*.

ROOPA

The true onset of the disease is identified by the emergence of its signs and symptoms. *Vyakthavastha* of *Shatkriyakala* is where those signs & symptoms are present. Different authors explained clearly about the *Lakshanas* of each *Mutrakrichra* on the basis of *Dosha* predominance. *Krichramutrata*, *Muhurmuhur Mutra Pravritti, Basti Shoola, Mootradaha, Sarakta Mutrata, Saruja Mutrata*, and *Peeta Mootrata* are the characteristic signs of *Pittaja Mutrakrichra*, signifying the full manifestation of the disease.

Classification of Mutrakrichra

Table No. 2: Mutrakrichra Classification according to different authors

Sl.No.	Prakaras	Ca[12]	Su[13]	Ah[14]	As[15]	Mn[16]	Bp[17]	Yr[18]
	Vataja	+	+	+	+	+	+	+
	Pittaja	+	+	+	+	+	+	+
	Kaphaja	+	+	+	+	+	+	+
	Sannipataja	+	+	+	+	+	+	+
	Rakthaja	+	-	-	-	-	-	-
	Ashmarijanya	+	+	-	-	+	+	+
	Sharkarajanya	+	+	-	-	+	+	+
	Pureeshajanya	-	+	-	-	+	+	+
	Sukrajanya	+	-	-	-	+	+	+
.	*Shalyabhighataja*	-	+	-	-	+	+	+

UPASHAYA AND ANUPASHAYA

"*Upashaya*" specifies factors that reduce symptoms, and "*Anupashaya*" specifies factors that exacerbate them. These can include *Vihara* (lifestyle practices), *Ahara* (diet), and *Aushadha* (medications). The *samhitas* make no direct reference to *Upashaya* and *Anupashaya* in the context of *Mutrakrichra*. However, measures that reduce or aggravate pitta—since *Mutrakrichra* is a *Pitta*-dominant condition—can be considered as *Upashaya*

and *Anupashaya*. In other words, *Pathyas* and *Apathyas* can be viewed as *Upashaya* and *Anupashaya*, respectively.

SAMPRAPTI

"*Samprapti*" refers to the stage that illustrates the involvement of *Doshas*, *Dhatus*, and *Malas*. It is the systematic process that outlines the progression from *Nidanasevana* to the manifestation of the disease. The treatment lies in disrupting the process of *Samprapti* itself, as stated in the principle, "*Samprapti Vighatanameva Chikitsa*." The imbalanced Doshas settle in the Basti, either individually or collectively, causing various disorders in the *Mutrashaya*, *Mutramarga*, and the process of micturition, which ultimately lead to different types of *Mutravikaras*.

Samprapti Ghataka

Dosha: *Pitta Pradana Tridosha.*

Dushya: *Mutra*

Agni: *Jataragni*

Ama: *Jataragnimandyajanya*

Srotas: *Mutravaha srotas*

Udbhava Sthana: *Amapakwashaya*

Sanchara Sthana: *Mutravaha sroto marga*

Adhistana: *Mutravaha srotas /basti*

Vyakta sthana: *Mutramarga*

Rogamarga: *Madhyama*

The *Drava Dhatus* are diminished by *Pitta* due to its *Ushna, Teekshna* and *Katu Guna*, by *Vata* due to its *Rooksha* and *Sookshma Guna* and by *Kapha* its *Avarodha*. *Dushya* comprises of *Dhatus*, *Upadhatus* and *Malas*. *Rasa, Rakta, Udaka* and *Mutra* are the main *Drava Dhatus* in the causation of the *Mutrakrichra*. The diminished Drava Dhatus lead to scanty urine. Diminution of *Jataragni* is responsible for the *Shoshana* of *Drava Dhatu* resulting in change of urine quality. This *Alpabala* of *Agni* is produced *Ama*. The *Ama* lodges in the place of *Khavaigunya* to cause *Srothorodha*. *Udhabavastana* is *Amapakwashaya* and *Samprapti* takes place in the *Basti*. So, it is considered as *Adhishtana* of *Mutrakrichra*.[61 62]

UPADRAVA[19]

The *Upadravas* of Mutrakrichra include *Karshya, Arati, Aruchi, Sanavasthiti, Trishna, Shoola, Vishada*, and *Arti*, as described in the *Kashyapa Samhita, Chikitsa Sthana*.

Sadhyasadhyata[20]

If *Mutrakrichra* is newly started, it is curable. If it is become chronic, it becomes *Yapya* or *Krichrasadhya* (curable with difficulty). *Acharya Charaka* opines that "incurable diseases never becomes curable while curable disease may pass into the stage of incurable on account of the short comings in any of the four basic therapeutic factors or as the result of destiny". This principle is applicable to *Mutrakrichra* also. *Acharyas* have mentioned only prognosis of *Sannipatika Mutrakrichra* as *Krichrasadhya* and *Ashmarijanya Mutrakrichra* as *Shastra Sadhya* or *Sashta Sadhya*[21]

URINARY TRACT INFECTION

DEFINITIONS

Urinary Tract Infection is defined as a condition in which the bacteria invade, persist and multiply within the urinary tract. It is termed as bacteriuria, as the presence of detectable bacteria in the sample of urine.

Acute urinary tract infections can be classified into two main anatomic categories: lower tract infections (such as urethritis and cystitis) and upper tract infections (including acute pyelonephritis, prostatitis, intrarenal, and perinephric abscesses).

Infections of the urethra and bladder are often considered superficial infections, while prostatitis, pyelonephritis and renal suppuration signifies tissue invasion. From a microbiologic perspective, urinary tract infection (UTI) exists when pathogenic microorganism is` detected[22].

EPIDEMIOLOGY

Epidemiologically, UTIs are subdivided into catheter associated infections and non-catheter-associated infections. Infections in either category may be symptomatic or asymptomatic. These infections occur in 1 to 3% of schoolgirls and then increase markedly in incidence with the onset of sexual activity in adolescence. Acute symptomatic UTIs are unusual in men under the age of 50. The development of asymptomatic bacteriuria parallels that of symptomatic infection and is rare among men under the age of 50, but common among women between 20 and 50. Asymptomatic bacteriuria is more common among elderly men and women, with rates as high as 40 to 50%.[23]

ETIOLOGY

Many different microorganisms can infect the urinary tract, but by far the most common agents are the gram-negative bacilli. Escherichia coli causes 80% of acute infections in patients without catheters, urologic abnormalities, or calculi. Other gram-negative rods, especially proteus and Klebsiella and occasionally Enterobacter, account for a smaller proportion of uncomplicated infection. Gram positive cocci plays a lesser role in UTIs. Few viruses can also be isolated from urine, e.g.: cytomegalovirus.[24]

CLINICAL PRESENTATION

Acute Pyelonephritis

Acute Pyelonephritis presents as classic triad of loin pain, fever, and tenderness over the kidneys. Microscopically they show focal inflammatory reaction with neutrophil and monocyte infiltration, tubular damage and interstitial edema. During the acute stage of the illness, haematuria may be seen. Even after receiving antibiotic treatment, fever in severe pyelonephritis subsides slowly and may persist for several days.[25]

Acute Bacterial Cystitis

This is the most common type of urinary tract infection in females. In addition to *E. coli*, *Staph. Saprophyticus* infection may be encountered in few cases. The typical symptoms are dysuria, increased frequency, urgency, voiding small volumes of urine and lower abdominal and suprapubic pain. The urine often becomes grossly cloudy and malodorous and is bloody in ~30% of cases. White cells and bacteria can be detected by urine examination.[26]

Urethritis

Clinically, women infected with cystitis should be distinguished from women infected with low-count E. coli/Klebsiella pneumoniae infection of urethra and bladder. Gross hematuria, suprapubic pain, an abrupt onset of illness, a duration of illness of <3 days and a history of UTIs favour the diagnosis of UTI.[27]

Catheter-Associated UTIs

At least 10–15% of hospitalised patients with temporary indwelling urethral catheters develop bacteriuria. It has been repeatedly demonstrated that the most frequent cause of gram-negative bacteraemia in hospitalised patients is the catheterised urinary tract. These infections are typically caused by E. Coli, Klebsiella, Proteus, and Candida. Female gender, extended catheterisation, disconnecting the catheter and drainage tube, and not receiving systemic antibiotic medication are all factors linked to an elevated risk of catheter-associated UTI. Infection results from bacteria spreading to the bladder through the urine column in the catheter lumen (intraluminal route) or up the mucosal sheath outside the catheter (periurethral route).[28]

DIAGNOSTIC TESTING

Determination of number and type of bacteria in the urine is extremely important diagnostic procedure. In symptomatic patients, bacteria are usually present in the urine in large numbers. Since the large number of bacteria in the bladder urine is due in part to bacterial multiplication during residence in the bladder cavity, samples of urine from the ureters or renal pelvis may contain $<10^5$ bacteria per millilitre and yet indicate infection. The detection of bacteria by microscopy indicates infection, but the absence of microscopically detectable bacteria does not exclude the diagnosis. Pyuria is demonstrated in nearly all acute bacterial UTIs. Pyuria in the absence of bacteriuria (sterile pyuria) may indicate infection with unusual agents such as C. trachomatis, U. urealyticum or Mycobacterium tuberculosis. Urine culture and antimicrobial susceptibility testing be performed for any patient with a suspected UTI.[29]

IV. DISCUSSION

Mutrakrichra is an important *Mutravaha Srotovikara* described in Ayurveda, characterized by difficulty and pain during micturition. Among its variants, *Pittaja Mutrakrichra* exhibits features such as *krichra mutrata, muhurmuhur pravrutti, mutradaha, saruja, sarakta* and *peeta mutra*, which closely resemble the clinical presentation of lower urinary tract infection (UTI).

The etiological factors described for *Mutrakrichra*, including excessive intake of *katu*, *amla*, and *lavana rasa*, *madya sevana*, *rooksha ahara*, *adhyashana*, *ajeerna bhojana*, *teekshna oushadha sevana*, and *vegadharana*, are predominantly *Pitta-prakopaka*. These factors lead to increased urine concentration, alteration of urinary pH, and irritation of the *Mutramarga*, creating favorable conditions for microbial growth, comparable to the pathogenesis of UTI.

In *Pittaja Mutrakrichra*, vitiated *Pitta Dosha*, along with *Vata* and *Kapha*, lodges in the *Mutravaha Srotas* due to *Khavaigunya*, resulting in *Dosha-Dushya Samurchana*. The involvement of *Drava Dhatus* (*Rasa*,

Rakta, *Udaka*, and *Mutra*) explains symptoms such as burning micturition, dysuria, hematuria, and urinary frequency, which parallel inflammatory changes seen in cystitis and urethritis.

The absence of clearly defined *Purvarupa* may be correlated with the acute onset of UTI, where symptoms rapidly progress to the manifest stage. The *Samprapti Ghatakas—Pitta-pradhana Tridosha*, *Mutra* as *Dushya*, *Mutravaha Srotas* involvement, and *Basti* as *Adhishtana*—further support this correlation. Prognostically, the *Sadhya* nature of early *Mutrakrichra* and *Krichrasadhyata* of chronic cases aligns with the clinical course of uncomplicated and recurrent UTIs.Thus, *Pittaja Mutrakrichra* can be effectively correlated with lower urinary tract infection based on similarities in etiology, clinical features, pathogenesis, and disease progression, highlighting the relevance of Ayurvedic concepts in understanding urinary tract disorders.

V. CONCLUSION

The present review highlights a close correlation between *Pittaja Mutrakrichra* described in Ayurveda and lower urinary tract infection as understood in contemporary medicine. Similarities in etiological factors, clinical manifestations, pathogenesis, and disease progression indicate that *Pittaja Mutrakrichra* can be considered the Ayurvedic counterpart of lower urinary tract infection. The predominance of *Pitta Dosha*, involvement of *Mutravaha Srotas*, and manifestation of symptoms such as dysuria, burning micturition, urinary frequency, and hematuria further strengthen this correlation. Understanding urinary tract infection through the Ayurvedic framework of *Pittaja Mutrakrichra* provides a comprehensive perspective and may help in adopting preventive and therapeutic strategies based on Ayurvedic principles for effective management of urinary tract disorders

VI. REFERENCES

1.Paradkar H. Sarvangasundara commentary of Arunadatta on Astanga hridayam of Vagbhata and Ayurvedarasayana of Hemadri, Sutra Sthana chapter 11, verse 1. Varanasi: Krishnadas Academy, Edition: Reprint 2009. pg no.182

2. Paradkar H. Sarvangasundara commentary of Arunadatta on Astanga hridayam of Vagbhata and Ayurvedarasayana of Hemadri, Sutra Sthana chapter 11, verse 5. Varanasi: Krishnadas Academy, Edition: Reprint 2009. pg no.183

3. Paradkar H. Sarvangasundara commentary of Arunadatta on Astanga hridayam of Vagbhata and Ayurvedarasayana of Hemadri, Sutra Sthana chapter 4, verse 1. Varanasi: Krishnadas Academy, Edition: Reprint 2009. pg no.52

4. Acharya Y T, editor (5th ed.). Ayurveda Dipika commentary by Chakrapanidatta on Charaka Samhitha of Agnivesha revised by Charaka & Dridabala, Chikitsa Sthana; Trimarmiya Chikitsadhyaya: Chapter 26, verse 34. Varanasi: Choukhamba Sanskrit Sansthan, 2001; pg no.599

5. Editor(s), compiler(s) :Colledge N.R, Boon N.A, Walker B.R,Editors. Davidson's

Principles and Practice of Medicine. 21st edition. China: Elsevier Limited; 2010: p.469

6. Datta C. Chakradatta with Padarthabodhini Hindi commentary. Edited by Ravidatta Shastri V. Varanasi: Choukambha Surabharati Prakashana; 2000. p. 144–145.

7. Agnivesa. Charaka Samhita, Chikitsa Sthana, chapter 26, sloka 32. 4th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1994. (Kasi Sanskrit Series) p. 228

8. Madhavakara, Madhavanidana chapter 30 sloka 1. Varanasi: Chaukhambha Surbharathi Prakashan; 1998. (Chaukhambha Ayurvijnana Granthamala) p. 46.

9. Bhavamishra, Bhavaprakasha Madhyamakhanda chapter 35 sloka 1. 5th ed. Varanasi: Chaukhambha Orientalia; 1988. (Chaukhambha Sanskrit series) p.130.

10. Yogaratnakara Mootrakrichra nidana sloka 1. Vaidya Lakshmipatisastry editor. Varanasi: Chaukhambha Sanskrit Sansthan; 1988. (Kasi Sanskrit series) p.160

11. Agnivesa. Charaka Samhita, Sutra Sthana, chapter 26, sloka 32. 4th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1994. (Kasi Sanskrit Series) p. 228.

12. Agnivesa, Charakasamhitha Chikitsasthana chapter 26 sloka 32. 4th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1994. (Kasi Sanskrit series 228).

13. Sushrutha, Sushruthasamhitha Uttarathantra chapter 59 sloka 3. Varanasi: Krishnadas Academy; 1980. (Krishnadas Ayurveda series 51).

14. Vagbhata, Ashtangahridaya Nidanasthana chapter 9 sloka 6. Varanasi: Krishnadas Academy; 1982. (Krishnadas Academic series 4).

15. Ashtangasangraha Nidanasthana chapter 9 sloka 3. Prof.K.R.Shrikhantamurthy editor. Varanasi: Chaukhambha Orientalia; 1996. (Jaikrishnadas Ayurvedic series 79).

16. Madhavakara, Madhavanidana chapter 30 sloka 2. Varanasi: Chaukhambha Surbharathi Prakashan; 1998. (Chaukhambha Ayurvijnana Granthamala) p. 46.

17. Bhavamishra, Bhavaprakasha Madhyamakhanda chapter 10 sloka 2. 5th ed. Varanasi: Chaukhambha Orientalia; 1988. (Chaukhambha Sanskrit series) p.130.

18. Yogaratnakara Mootrakrichra Nidana sloka 10. Vaidya Lakshmipatisastry editor. Varanasi: Chaukhambha Sanskrit Sansthan; 1988. p. 51. (Kasi Sanskrit series) p.160.

19.Agnivesa, Charakasamhitha chikitsasthana chapter 26 sloka 33. 4th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1994. (Kasi Sanskrit series) p.228.

20. Madhavakara, Madhavanidana chapter 30 sloka 2. Varanasi: Chaukhambha Surbharathi Prakashan; 1998. (Chaukhambha Ayurvijnana Granthamala) p.46.

21. K Vrudhajeevaka, Kashyapasamhita Chikitsasthana chapter 10 sloka12-13. 4th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1988. (Kasi Sanskrit series) p.154.

22. Agnivesa, Charakasamhitha sutrasthana chapter 10 sloka 11-20. 4th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1994. (Kasi Sanskrit series p.228

23. Sushrutha, Sushruthasamhitha Uttaratantra chapter 59 sloka 28. Varanasi: Krishnadas Academy; 1980. (Krishnadas Ayurveda series) p.51.

24. Fauci AS, Kasper DL, Longo DL, editors. *Harrison's Principles of Internal Medicine*. 16th ed. Vol. 2, Part 14. New York: McGraw-Hill; 2004. p. 1715.

25. Fauci AS, Kasper DL, Longo DL, editors. *Harrison's Principles of Internal Medicine*. 16th ed. Vol. 2, Part 14. New York: McGraw-Hill; 2004. p. 1715.

26. Fauci AS, Kasper DL, Longo DL, editors. *Harrison's Principles of Internal Medicine*. 16th ed. Vol. 2, Part 14. New York: McGraw-Hill; 2004. p. 1715.

27. Fauci AS, Kasper DL, Longo DL, editors. *Harrison's Principles of Internal Medicine*. 16th ed. Vol. 2, Part 14. New York: McGraw-Hill; 2004. p. 1717.

28. Fauci AS, Kasper DL, Longo DL, editors. *Harrison's Principles of Internal Medicine*. 16th ed. Vol. 2, Part 14. New York: McGraw-Hill; 2004. p. 1717.

29. Fauci AS, Kasper DL, Longo DL, editors. *Harrison's Principles of Internal Medicine*. 16th ed. Vol. 2, Part 14. New York: McGraw-Hill; 2004. p. 1717.