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Timely Diagnosis of Testicular Cancer

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Screening for testicular cancer, like any true disease-screening effort, involves evaluation of an asymptomatic population for the disease in question. The goal of any cancer screening effort is to diagnose the disease at an early, more easily treatable stage with the ultimate goal of improving the disease-specific survival and minimizing treatment morbidity. Screening efforts can also be directed toward population groups most at risk for the disease to improve cost effectiveness, which is becoming increasingly important as we face the aging of the "Baby Boom" generation.

Although testicular cancer is an uncommon neoplasm, it is the most common solid tumor in men between the ages of 20 and 34, and the incidence is increasing [1]. Because of the known and continuing problem of delayed diagnosis, which is discussed later, screening might be considered for this disease. Conversely, with most patients now being cured, the screening goal of increasing disease-specific survival may be impossible to improve substantially. The goal of early detection to minimize morbidity of treatment may be an obtainable goal.

Particularly relevant to testicular cancer is the concept of true screening of an entire asymptomatic population versus case finding in at-risk or symptomatic men. Akin to case finding is the concept of testicular self-examination (TSE) and increasing awareness of this disease among young men.

Importance of early detection

The common sense importance of early detection and diagnosis of testicular cancer has been known for many years. Before the advent of curative therapy, this was one of the few ways (if not the only way) to prevent deaths in the usually young and otherwise healthy men who are affected. In the current era of effective chemotherapy, most (but not all) patients can be salvaged despite delays in diagnosis and, consequently, more advanced disease [2]. This salvage, however, generally requires much more extensive chemotherapy or surgery, and the potential morbidity of these more heroic efforts must not be underestimated. Expedient diagnosis of these neoplasms affords the opportunity to treat these patients at their earliest stage of disease and therefore to minimize long-term morbidity.

Despite this worthy goal of early diagnosis, pitfalls in the early and accurate diagnosis of testicular tumors are common. Delay in diagnosis of testicular cancer is well documented [2–30]. Table 1 illustrates that the mean delay (26 weeks) has varied little over the last 75 years from various series throughout the world. It is interesting that this approximate 5-month delay from initial symptoms to a surgical diagnosis has remained constant in these reports. Despite this consistency, some investigators have shown a trend toward a decreased delay in more recent years [2,12]. Dieckmann and colleagues [12] found that the number of patients in whom diagnosis was made improved within 2 weeks from 13.6% to 25.4% between 1969 to 1976 and 1982 to 1986. Similarly, Moul and colleagues [2] found that the mean symptomatic interval decreased from 22.7 to 16.4 weeks between the 1970 to 1974 and the 1985 to 1987 intervals. Conversely, Nikzas and colleagues [22] found no decrease in delay between 1980 and 1987 in 232 patients studied in Great Britain. Even if delay time has improved somewhat, in some series it remains a significant

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Table 1
Delay in diagnosis of testicular cancer: review of the literature

Study	Time period of review	No. of patients	Mean duration of symptoms (wk)
Weissbach et al [3]	1926–1973	182	40
Host and Stokke [4]	1932–1953	289	33.6
Patton et al [5]	1940–1956	510	20
Thompson et al [6]	1940–1960	178	87
Bosl et al [7]	1941–1978	335	12
Kurohara et al [8]	1945–1965	196	25.4
Borski [9]	1953–1973	150	26.1
Seib et al [10]	1960–1973	50	20
Ware et al [11]	1965–1977	100	17.3
Dieckmann et al [12]	1969–1986	156	24.3
Kulig [13]	1970–1979	27	24
Moul et al [2]	1970–1987	148	21.1
Leyh [14]	1971–1982	101	21.8
Kuhne et al [15]	1971–1982	50	30.5
Scher et al [16]	1972–1979	123	8
Fischer [17]	1973–1981	182	20
Heising [18]	1976–1981	1344	19.6
Jones and Appleyard [19]	1976–1982	121	19.8
Thornhill et al [20]	1980–1985	217	40
Chilvers et al [21]	1980–1986	257	16
Nikzas et al [22]	1980–1987	232	22
Total	—	4948	26

problem. Patients and health care providers may contribute to delay in diagnosis. Patient-mediated delays owing to ignorance, embarrassment, fear of cancer, or fear of emasculation are well known [23,28]. Dieckmann and colleagues [12] found that delay was related to educational level. College-educated men in whom both seminoma and nonseminoma were diagnosed were found to have shorter mean and median delays. The less informed or less educated patient may actually believe that a larger testicle makes a more virile man [23]. Patients who have testicular cancer may be more inclined than other cancer patients to delay or even refuse seeking medical attention or treatment [31]. Testicular cancer affects young and usually otherwise healthy men who may be unable to acknowledge the threat of fatal disease. Instead of seeking evaluation, they may hold fast to their normal routine as a denial mechanism termed the *flight into health* [32]. Furthermore, that testicular cancer involves the loss of an external sexual organ during a time in the patient's life when sexuality is very important is an added stressor [31]. Jones and Appleyard [19] point out that it is often the partner and not the patient himself who insists that medical attention be sought.

Physician-mediated delay most commonly results from the misdiagnosis of a testis tumor as an infection. Unfortunately for the clinician, the classic painless testicular mass or swelling is the presenting symptom in only approximately half of patients in whom testicular cancer ultimately is diagnosed (Table 2). Scrotal pain with or without a mass occurs in up to 50% of testicular cancer presentations and has been attributed to hemorrhage into the tumor [5,25,33].

This painful presentation is not uncommonly responsible for a false diagnosis of epididymitis. In one study of 335 testicular cancer patients, one third were treated initially with antibiotics or local treatments for presumed epididymitis, and most of these were delayed from appropriate orchiectomy for more than 2 weeks [7]. In another study of 133 men who had testicular cancer, 23 (17%) were treated initially for epididymitis [26]. Most were delayed for 2 or 3 months, and 5 patients were delayed from 6 to 22 months.

Because nonseminomas generally are considered a more rapidly growing neoplasm than seminomas, they may be more commonly associated with a painful presentation. Sandeman [24] found that 109 (47%) nonseminoma patients initially presented with pain, whereas only 102 (38%) seminoma patients had a similar presentation. Seminomas are usually a more indolent-growing neoplasm, and a painless mass or swelling is the most common presentation. It is the nonseminoma patient who might benefit the most from early diagnosis but who also may be more difficult to distinguish from a patient who has an inflammatory lesion.

In my prior practice at the Walter Reed Army Medical Center and now at Duke University, we frequently see young men who are prime candidates for testicular cancer or epididymitis. Our policy is to assume malignancy until proved otherwise. Urinalysis usually demonstrates pyuria when epididymitis is present and, in most cases, epididymal tenderness and swelling are distinguishable from the testis proper. When more severe orchitis or swelling is present and suspicion for tumor persists, a 1% lidocaine cord block can allow for a more meaningful examination. If we

Table 2
Presenting signs and symptoms of testicular tumors in various series

Signs and symptoms	Percentage presenting							
	Patton et al [5] (n = 491)	Robson et al [33] (n = 360)	Sandeman [24] (n = 502)	Bosl et al [7] (n = 335)	Dieckmann et al [12] (n = 180)	Thornhill et al [20] (n = 217)	Wishnow et al [27] (n = 154)	Meffan et al [30] (n = 79)
Painless mass or swelling	NS	56.9	54	NS	51.2	32	57	43
Painful scrotum with or without mass or swelling	NS	26.4	42	45	32.8	31	40	50
Incidental finding	5	4.3	4	NS	NS	23	NS	NS
Associated with trauma	7	13[a]	NS	11.2[b]	NS	10	NS	3
Symptoms and signs of metastases	10	5.2	NS	10.7	6.3	19	NS	5
Gynecomastia or tenderness	NS	NS	NS	5	1.1	2	3	1.3

Abbreviation: NS, not stated.
[a] Hernia, traumatic orchitis, or torsion.
[b] Trauma, hydrocele, or benign tumor.

still have any index of suspicion for a tumor, we proceed directly to scrotal sonography.

Serum tumor markers, such as β–human chorionic gonadotropin and α-fetoprotein, usually are also useful to obtain in this setting and are absolutely essential to obtain before orchiectomy. The differential diagnosis of testicular masses has been aided by cytologic examination of seminal fluid obtained by ejaculation or prostatic massage [34,35]; however, this is not in widespread clinical use. Even if the clinician is sure of a diagnosis of epididymitis or orchitis, it is still prudent to insist that the patient be seen in follow-up in 7 to 10 days after the inflammation has subsided to re-examine the testis for an occult neoplasm. This follow-up of presumed infection is crucial especially if the diagnosis of epididymitis is not certain.

In addition to presumed infection, trauma frequently may cloud an accurate and early diagnosis of testicular cancer. Stephen [25] cites trauma as "a wolf in sheep's clothing" with respect to complicating the diagnosis of testicular cancer. Up to 10% of testicular cancer patients initially receive a diagnosis of posttraumatic pain or swelling (see Table 2). It is presumed that the enlarged tumorous testis is more susceptible to trauma or that less significant trauma might more easily precipitate symptoms. Patton and colleagues [5] claim that the trauma is coincidental in attracting the patient's attention to an already existing lesion. Stephen [25] has described an interesting sign whereby the lack of sickening pain at the moment of injury, because of prior destruction or partial destruction of the testis from neoplasm, is an important point to elicit from the patient. The pitfall is a less-than-adequate evaluation for tumor in a patient presenting with trauma. One should be especially wary when the swelling or pain is out of proportion to what would be considered minor trauma, or vice versa. Again, in the setting of trauma, a high index of suspicion for tumor is necessary and scrotal sonography, exploration, or compulsive follow-up frequently is indicated.

Up to 19% of patients present with signs or symptoms of metastases (see Table 2). Back pain, abdominal mass, lymphadenopathy, and weight loss are the most prevalent constitutional symptoms. An additional 1% to 5% of patients present with gynecomastia or breast tenderness. The major pitfall in these presentations is to fail to examine the genitalia and so miss an obvious testicular tumor, and thereby delay, misdiagnose, or mistreat a metastatic germ cell cancer. Oliver [28] has stated that the most severe delays in diagnosis occur in patients undergoing investigation of symptoms that are subsequently shown to have been caused by metastases. Inappropriate laparotomy in the case of an obvious testicular tumor remaining in situ is not rare [23]. Patients who have back pain have been subjected to osteopathic therapy while a testicular cancer went unsuspected [26]. Prout and Griffin [26] have even reported two patients being subjected to mastectomy for gynecomastia before any evaluation for testicular

cancer. Surprising as this may be, we have also seen a patient who had bilateral subcutaneous mastectomy and soon thereafter received a diagnosis of obvious testicular cancer [36].

For seminoma patients, delay in diagnosis is not necessarily associated with more advanced disease or decreased survival. Many investigators have noted that seminomas can have a protracted indolent growth, and symptom duration does not correlate with disease stage [2,12,24]. Because of slow growth characteristics, stage I seminoma can be associated with very long symptomatic intervals. Moul and colleagues [2] found the mean symptomatic interval for stage I seminomas to be 39 weeks, whereas that for stage II disease ranged from 11 to 18.5 weeks. Dieckmann and colleagues [12] found that stage I patients had a 228-day mean delay in diagnosis, compared with 129 days for the stage II seminomas. Regarding survival and delay for seminoma patients, the longer period of delay has not been shown statistically to affect survival, although deaths from seminoma have been associated with very long delays [2].

For the nonseminoma patient, there is a clearer association between delay in diagnosis and advanced disease. Bosl and colleagues [7] found a median delay of 75, 101, and 134 days for stages I, II, and III testicular cancer, respectively (24% seminomas included). Thornhill and colleagues [20] noted that stage I patients had a mean duration of symptoms of 2.2 months, whereas stage II cases were delayed 4.7 months (stage III and IV were delayed 3.4 and 4.5 months, respectively). Chilvers and colleagues [21], reporting on 257 nonseminomatous germ cell tumor (NSGCT) patients seen between 1980 and 1986, found that of those who sought medical advice within 100 days of onset of symptoms, 54% had stage I tumors compared with 41% who delayed longer ($P = .05$ by χ^2 analysis). The Wishnow and colleagues [27] study of 154 NSGCT patients compared patients in whom tumor was diagnosed within 1 month (n = 65, group 1) to patients delayed longer than 1 month (n = 89, group 2). Sixty-two percent of group 1 presented with stage I disease compared with only 28% of group 2 ($P < .001$). Similarly, only 8% of group I patients had stage III disease, compared with 39% of group 2 patients ($P < .001$, χ^2). Moul and colleagues [2] found the mean symptomatic interval for stages I, IIA, and IIB nonseminomas to range between 8.5 and 9.7 weeks, whereas for stages IIC and III the delay was 26.4 weeks.

Increased delay has also traditionally been associated with decreased survival for nonseminoma patients. Sandeman [24] reported a progressively decreased 3-year disease-free interval as delay increased. Post and Belis [23] reported a 69% 3-year survival for patients in whom NSGCT was diagnosed within 3 months, versus a 47% survival if the delay was greater than 3 months. Prout and Griffin [26] noted a 0% crude death rate for men in whom diagnosis was made within 1 month, compared with a 27.6% death rate when delay was longer than 1 month. Oliver [28] found that the average delay was 2 months in patients who remained free of disease, 4 months in those who relapsed but were salvaged, and 7 months in those who died of drug-resistant disease. Thornhill and colleagues [20], studying 217 cases of testicular cancer in Ireland, found delay to be statistically associated with metastases, diminished prospects of cure, and mortality. The median duration of symptoms was 4 months in those who died of disease, compared with 2.5 months in those patients who were alive. Wishnow and colleagues [27] noted that only 1 of 65 patients in whom diagnosis was made within 1 month died of disease, whereas 11 of 89 (12.4%) delayed beyond 1 month died of testicular cancer ($P = .0072$, χ^2). In a study of 232 patients treated between 1980 and 1987, Nikzas and colleagues [22] found an 8% mortality in patients in whom tumor was diagnosed within 6 months, compared with 16% in those with a longer delay ($P < .01$).

Moul and colleagues [2] found that a delay greater than 16 weeks had a strong statistical adverse effect on survival for nonseminoma patients treated between 1970 and 1987. When these investigators separated patients treated during the more contemporary "cisplatin era" (1979–1987), the impact of delay on survival was attenuated and no longer was statistically significant. These authors concluded that effective chemotherapy salvages many patients who in the past would have been at a disadvantage as a consequence of delayed diagnosis. Other investigators also have found that delay in diagnosis does not necessarily influence survival for NSGCT patients in the contemporary era. In their study of 257 NSGCT patients between 1980 and 1986, Chilvers and colleagues [21] actually found an inverse relationship between delay and survival. Patients in whom diagnosis was made within 0 to 49 days had a lessened relapse-free survival compared with patients in whom diagnosis was made later ($P < .05$, log rank test for trend). The authors concluded that

faster-growing, more aggressive tumors are more likely to produce symptoms leading to medical consultation. Similarly, Meffan and colleagues [30], in a small study of 79 patients (40 seminomas, 39 NSGCT) treated between 1976 and 1985 in New Zealand, found no relation between delay and prognosis. They concluded that all cases in their series were being diagnosed too late and that is why no association was seen.

Although contemporary chemotherapy may salvage most patients despite delay in diagnosis and more advanced disease, deaths still result from delay. Furthermore, effective chemotherapy may be a double-edged sword in that clinicians may become more lax in expediently caring for these patients and so delay may increase [27]. The potentially higher morbidity associated with the more intensive therapy that is required to salvage patients as a consequence of delay must not be underestimated. Efforts to decrease delay in diagnosis may be the most cost-effective method to improve further the survival of testicular cancer patients and to lessen treatment morbidity.

True screening

True screening would involve evaluating an entire asymptomatic population for testicular cancer. With the overall high curability and low incidence of this disease, it is debatable whether we should invest in screening programs for testicular cancer. The principal screening test for testicular cancer is palpation of the testis by an examiner [37]. The sensitivity, specificity, and positive predictive value of the testicular examination in asymptomatic individuals are unknown. False-negative and false-positive examinations because of epididymal and testicular changes from infections, trauma, and cysts are common even among urologists and would be significantly higher among other practitioners. Varicoceles and hydroceles, relatively common conditions, also would pose accuracy problems for screening physical examinations. Alternatively, scrotal sonography might be more accurate in general widespread screening, but the cost-effectiveness of this modality for this uncommon neoplasm is questionable [38].

Despite these concerns regarding testicular examination, the American Cancer Society and the National Cancer Institute [39,40] recommend that it be included as part of the periodic health examination of men. The Canadian Task Force and the US Preventive Services Task Force, however, recommend that screening examinations should be performed only on patients who have risk factors, such as those with a history of cryptorchidism or testicular atrophy [37,41]. Aside from age, the only currently known main risk factors for testicular cancer include cryptorchidism, Caucasian race [42], prior testicular tumor, and family history. Screening of these risk groups may be beneficial, although the value has not been proved.

Because of the rarity of this disease and the inaccuracy of the screening test (scrotal examination by physician), routine screening examinations of the genitalia of all asymptomatic men would have a low yield and would not be cost effective. From the available information, general screening of the population is not indicated, but a testicular examination should be part of the male physical examination, and periodic screening for men with risk factors may be beneficial.

Case finding and testicular self-examination

Case finding is similar to screening but involves detecting disease in a symptomatic patient or one who presents to the physician with concerns that he might have the disease in question. As can be surmised from the prior discussion regarding delay in diagnosis, case finding for testicular cancer is critically important for the man who presents with scrotal symptoms, such as a mass, pain, or swelling, or after trauma. As previously noted, testicular cancer should not be overlooked when initial signs or symptoms are related to distant metastases. Case finding may be enhanced by patient education about testicular cancer and by TSE.

TSE is the process of instructing patients to examine themselves periodically for testicular masses, swelling, and other changes, and is patterned on the well-accepted concept of breast self-examinations [43–56]. The American Cancer Society and the National Cancer Institute [57,58] recommend that all postpuberal males perform a monthly TSE. Not all authorities agree that TSE is beneficial, however. The US Preventive Services Task Force [37] contends that there is insufficient evidence for or against counseling patients to perform periodic TSE. This group contends that reliable information on the accuracy of TSE is lacking and that it is unknown whether counseling men to perform TSE actually motivates them to adopt the practice or to perform it correctly [37]. Others, citing the lack of evidence

that TSE is effective, advised physicians against routinely devoting time to discussing TSE [59,60]. Some have argued that the yield does not offset the increased anxiety that emphasis on TSE causes among men in an age group that already has many bodily concerns [47]. Conversely, Friman and Finney [61] point out that TSE would not cause excess anxiety but would reduce anxiety with regular practice. Furthermore, teaching young men to conduct TSE may result in these men taking increased responsibility for their own health care [61].

Despite the knowledge and perceived benefit of TSE by most health care professionals, little of this knowledge has been transferred to the public. Sheley and colleagues [62] studied 415 men from different regions of the United States and found that only 2% reported correctly performed, monthly TSE. These investigators concluded that there was a technology transfer problem regarding awareness of testicular cancer and TSE, teaching proper TSE, and conveying a benefit to the individual for performing TSE. Dachs and colleagues [63] similarly found that only 4.7% of New England college students performed monthly TSE in the mid-1980s. Even after being provided written material and a lecture on TSE by a physician, only 36% of the students changed their behavior and began performing monthly TSE [63].

Brubaker and Wickersham [64] postulate that the reason for this failure of TSE education is based on the theory of reasoned action, which proposes that performance of a behavior, such as TSE, is a direct result of a person's reasoned intention to perform that behavior. Behavioral intention, in turn, is a function of the individual's attitude toward the behavior and his or her perception of whether significant others would approve. Attitude toward the behavior reflects salient beliefs about the outcomes of performing the behavior, weighted by the value of each outcome. Brubaker and Wickersham [64] studied 232 college men exposed to educational lectures, reading materials, and posters about TSE. A student's attitude about the potential benefit of TSE and the perceived value of TSE by other peers affected his intention to perform TSE. Likewise, intention helped to determine who actually performed TSE. Clearly, we must convey a benefit to performing TSE to change a young man's intention to carry through with the behavior. Simple education without conveying a benefit of the behavior will not succeed in increasing the practice of TSE.

Having concluded that TSE may be beneficial at least for men who have risk factors for testicular cancer, if not for all young men, its teaching should emphasize the following points. First, men must gain familiarity with the surface, texture, and consistency of their testicles in the normal state. Second, the ideal time for TSE is during or after a warm bath or shower. Third, the man examining himself should rotate both testicles between thumb and forefinger until he determines that the entire surface of each is free of lumps. Fourth, the man should learn the location of the epididymis and that this structure is not a tumor. Fifth, any detected lump should be reported to a physician immediately [65]. Most importantly, as noted earlier, physicians must convey the benefit of TSE to affect the intention to perform it regularly. Education must include possible consequences of not performing TSE, such as delay in diagnosis with resulting advanced stage of disease; the need for intensive treatment, such as chemotherapy; and death. One approach may be to have a testicular cancer survivor discuss his experiences to convey the benefit of TSE [51]. Regarding the actual technical procedure itself, the message is that TSE is easily learned and should be practiced regularly [61]. Studies have shown that TSE teaching improves knowledge and performance of the self-examination [53,64,66].

Public awareness

Despite the controversy regarding physician-conducted screening and TSE, there seems to be a consensus that increased awareness about testicular cancer among young men is necessary [66]. Those who advocate TSE programs must be mindful that these cannot succeed unless education and awareness can impart a value to the behavior. Numerous recent studies have demonstrated that young men generally are ignorant regarding testicular cancer and TSE (Table 3). On average, less than two thirds of young men had ever heard of testicular cancer and only approximately one third knew that it primarily affects young men. Less than one third were aware of TSE, and less than 10% perform TSE [38,43,62,63,67–75]. Most of these studies were of college and graduate students, implying that the general population knows little or nothing about this disease [38,67–69]. The largest survey of more than 7,000 European students found that 87% never practiced TSE and only 3%

Table 3
Knowledge of testicular cancer among young people

Study	No. of subjects	Ever heard of testicular cancer (%)	Aware that young men are at risk (%)	Aware of TSE (%)	Practice of TSE (%)	Aware that testicular cancer usually is curable (%)
Conklin et al [43]	90	25	NS	0	0	NS
Cummings et al [67]	266	NS	42	16	5	NS
Goldenring and Purtell [38]	147	NS	13	9.5	6	NS
Thornhill et al [68]	365	68	13	8	1.3	14
Blesch [69]	129	61	NS	31	9.5	NS
Reno [70]	126	NS	NS	13	9.5	NS
Dachs et al [63]	633	NS	57	39	4.7	NS
Klein et al [71]	66	47	15	23	1.5	NS
Raghavan [72]	80	<15	10	NS	NS	NS
Pendered [73]	Men, 79	63	29	35	27	59
	Women, 96	72	50	48	—	82
Sheley et al [62]	415	NS	30	NS	16	NS
Singer et al [74]	717	NS	30	30	8	6
Wardle et al [75]	7,304	NS	NS	NS	9	NS

Abbreviation: NS, not stated.

reported regular monthly TSE [75]. Even among health care providers, knowledge is lacking. Stanford [54] found that almost one half of female nurses were not familiar with TSE, and only 5% had taught a patient TSE, although almost two thirds believed it to be part of their job.

Regarding knowledge of signs and symptoms of testicular cancer, Cummings and colleagues [67] also found that more than half of the young men in their study could not identify any correct signs or symptoms of testicular cancer (lump, swelling, enlarged and heavy testis, and pain). Similarly, Thornhill and colleagues [68] found 72% of young men had no knowledge of possible symptoms and actually noted many incorrect symptoms, such as problems with potency or micturition. In one study, young women knew more about testicular cancer than did men of similar age [73].

There are several patient-education brochures available that discuss not only TSE but also the general facts regarding this cancer. These materials are available from the American Cancer Society [57], the National Cancer Institute [58], the American Urological Association [76], and commercial sources [77].

Summary

Mass screening for testicular cancer using physician-conducted scrotal examinations or scrotal sonography is not indicated. Case finding by including a testicular examination as part of a male physical examination is recommended by the American Cancer Society and the National Cancer Institute. Self-screening by TSE may be effective, especially for patients at risk for testicular cancer, although educational efforts must also include and convey the potential value to the individual of such behavior. Awareness of testicular cancer and its signs and symptoms is abysmally poor in young men and undoubtedly contributes to the continued problem of delay in diagnosis. At a minimum, physicians must promote awareness so that men report to their physicians at the first sign or symptom of testicular pathology. Likewise, we must continue to promote education among health care providers.

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