Age-Appropriate Cancer Screenings Through a Dermatology Lens

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ABSTRACT

Background: Primary care physicians are often the first to identify signs and symptoms concerning for cancer. An important aspect of cancer screening is thorough skin examinations and subsequent referral to a dermatologist for atypical cutaneous presentations, which may be associated with an underlying visceral malignancy. Diagnostic considerations for pruritus without dermatitis ("itch without rash") in adults include senile pruritus, medication reaction, and paraneoplastic syndrome. Recognition of cutaneous manifestations of cancer should prompt cancer screening by primary care providers.

Objective: To update practicing physicians on current cancer screening guidelines with a specific focus on cutaneous clues to prompt further workup.

Methods: American Cancer Society and United States Preventive Services Task Force guidelines were systematically reviewed using PubMed and organizational websites during August and September, 2021, with review of Task Force Guidelines during October, 2022.

Results: Colorectal, cervical, breast, lung, skin, prostate, ovarian, hematologic, pancreatic, thyroid, testicular, bladder, oral, and gastric cancer screening guidelines are summarized.

Conclusions: Primary care physicians can recognize atypical cutaneous conditions and facilitate referral to a dermatologist for evaluation and/or directly order tests themselves to initiate appropriate cancer screening.

BACKGROUND

Primary care physicians are often the first to identify signs and symptoms concerning for cancer. An important aspect of cancer screening is thorough skin examinations and subsequent referral to a dermatologist for atypical cutaneous presentations, which may be associated with an underlying visceral malignancy. Diagnostic considerations for pruritus without dermatitis ("itch without rash") in adults include senile pruritus, medication reaction, and paraneoplastic syndrome. Recognition of cutaneous manifestations of cancer should prompt cancer screening by primary care providers.

With this review, we sought to update practicing physicians on current cancer screening guidelines with a specific focus on cutaneous clues to prompt further workup.

METHODS

American Cancer Society (ACS) and United States Preventive Services Task Force (USPSTF) guidelines were systematically reviewed using PubMed and organizational websites during August and September, 2021, with review of Task Force Guidelines during October, 2022.

Colorectal, cervical, breast, lung, skin, prostate, ovarian, hematologic, pancreatic, thyroid, testicular, bladder, oral, and gastric cancer screening guidelines are summarized (Tables 1 and 2).

CANCER SCREENING GUIDELINES

Colorectal Cancer Screening

As of May 2021, the United States Preventive Services Task Force (USPSTF) recommends colorectal cancer (CRC) screening in all adults aged 45-49 [Grade B] and 50-75 [Grade A].[1] Screening can be discontinued for patients aged 76-85 based on health status, prior screening results, or individual preference [Grade C].[1]

Notable risk factors include personal/family history of CRC or

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adenomatous polyps, inflammatory bowel disease, increased red meat intake, decreased fiber intake, inherited syndromes (such as Lynch syndrome), male sex, obesity, diabetes, smoking, or excess alcohol use.[1] Additionally, Black adults across all age groups have a higher incidence and mortality from CRC than White adults.[1]

There are several described cutaneous associations with underlying CRC. Leser-Trélat, dermatomyositis, acanthosis nigricans, tripe palms, Cronkhite-Canada syndrome, extramammary Paget's disease, and tripe palms are well-described associations and should prompt immediate colonoscopy.[2] Patients with Muir-Torre syndrome should begin CRC screening with colonoscopy every 1 to 2 years starting at age 25 (or 5 years prior to the youngest age of CRC diagnosis in the family) and annually at age 40.[3] A diagnosis of Peutz-Jeghers syndrome should prompt an esophagogastroduodenoscopy (EGD) and colonoscopy beginning at age 8, followed by a 1- to 3-year screening interval with colonoscopy if polyps are detected on baseline endoscopy.[4] Screening for CRC in patients with Gardner syndrome begins annually at ages 10-12, and proctocolectomy is indicated upon detection of 30 to 50 polyps in a single colonoscopy.[2]

Screening options include high-sensitivity guaiac fecal occult blood test (HSgFOBt) or fecal immunochemical test (FIT) every year, stool DNA-FIT test every 1 to 3 years, computed tomography (CT) colonography every 5 years, flexible sigmoidoscopy every 5 years or every 10 years plus an annual FIT test, colonoscopy every 10 years, or colonoscopy every 5 years with a family history of CRC or previous removal of adenomatous polyps.[1] When stool-based tests, flexible sigmoidoscopy, or CT colonography reveal abnormal results, follow-up colonoscopy is needed for validation.[1]

Cervical Cancer Screening

Cervical cancer screening is recommended every 3 years for women ages 21-29 via cervical cytology alone, regardless of sexual history or human papillomavirus (HPV) vaccination status [Grade A].[5] The USPSTF recommends cervical cancer screening every 5 years for women ages 30-65 with high-risk HPV testing in combination with cervical cytology (co-test) [Grade A].[5] Cervical cancer screening may be discontinued for women who had a hysterectomy with removal of the cervix or are over 65 years of age with negative results of screening on 3 consecutive tests or 2 negative co-testing results in the past 10 years.[6,7]

High-risk groups for cervical cancer include women with persistent HPV infections, a compromised immune system (HIV infection, organ transplant, and long-term steroid use), lack of health care access or health insurance coverage, cigarette smoking, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer.[5,7] New onset nodular skin lesions on the abdomen or vulva in patients with a history of cervical cancer should prompt referral to a dermatologist for biopsy to rule out metastasis.[7] Additionally, non-Hispanic Black women across all age groups have a higher incidence and mortality rate of cervical cancer than non-Hispanic White women.[8]

Breast Cancer Screening

The USPSTF recommends breast cancer screening with mammography every 2 years in women ages 50-74 [Grade B] and based on patient preference in women ages 40-49 [Grade C]; there is insufficient evidence to provide a recommendation for screening in women age 75 years and older [Grade I].[9] In contrast, the American Cancer Society (ACS) recommends screening with mammography annually in women ages 45-54, biennially in women ages 55 and older, and based on patient preference in women ages 40-44.[10] All major societies recommend screening with mammography every 1 or 2 years in women ages 50-74.[11] Notable risk factors include family history, early age radiation therapy to the chest, dense breast tissue, BRCA1 and BRCA2 gene mutations, inherited syndromes and existing but benign breast proliferative lesions with atypia. Men with BRCA1/2 mutations who have gynecomastia also should be screened.[12]

Dermatologic manifestations with links to breast cancer include mammary Paget's disease, Cowden syndrome, carcinoma en cuirasse, carcinoma erysipeloides, alopecia neoplastica, Sweet's syndrome, hypertrichosis lanuginosa acquisita, multicentric reticulohistiocytosis, dermatomyositis, acquired ichthyosis, erythema gyratum repens, and intralymphatic histiocytosis.[13,14]

Digital mammography is the gold standard for breast cancer screening. Adjuvant screening via ultrasonography, magnetic resonance imaging (MRI), and/or digital breast tomosynthesis may be considered in women identified to have dense breasts on an otherwise negative screening mammogram.[9]

Lung Cancer Screening

The USPSTF recommends screening patients ages 50-80 who have a history of smoking 20 packs/year and have quit smoking within the last 15 years or who currently smoke [Grade B].[15] The ACS recommends screening patients ages 55-74 who have a history of smoking 30 packs/year and have quit smoking within the last 15 years or who currently smoke.[16] Low-dose computed tomography (LDCT) without contrast is recommended for lung cancer screening.[15]

The greatest risk factors for lung cancer are older age and smoking history.[15] Other high-risk populations include Black males relative to White males and White females relative to Black females.[17] Dermatologic manifestations of lung cancer that should prompt screening include dermatomyositis, erythema gyratum repens, hypertrichosis lanuginosa, superficial thrombophlebitis (Trousseau syndrome), tripe palms, and Leser-Trélat.[18]

SKIN CANCER SCREENING

Screening for skin cancer via total body skin exam is among the

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Table 1. Age-Appropriate Cancer Screening Recommendations

Type of Cancer	Gender	Age	USPSTF Grade	Recommendation
Bladder	Female/Male	All ages	I	Insufficient evidence to recommend screening
Breast	Female	40-49	C	Screening per patient status/preference
Breast	Female	50-74	B	Screening mammography every 2 years
Breast	Female	75+	I	Insufficient evidence to recommend screening
Cervical	Female	21-65	A	Cervical cytology testing alone is recommend for women ages 21-29. High-risk human papilomavirus testing in combination with cervical cytology (co-test) is recommended for women ages 30-65
Colorectal	Female/Male	45-49	B	Screening recommended (annual HSgFOBt or FIT, DNA-FIT every 1-3 years, CT colonography every 5 years, flexible sigmoidoscopy every 5 years, flexible sigmoidoscopy every 10 years plus annual FIT test, or colonoscopy every 10 years)
Colorectal	Female/Male	50-75	A	Screening recommended (annual HSgFOBt or FIT, DNA-FIT every 1-3 years, CT colonography every 5 years, flexible sigmoidoscopy every 5 years, flexible sigmoidoscopy every 10 years plus annual FIT test, or colonoscopy every 10 years)
Colorectal	Female/Male	76-85	C	Screening per patient health status/preference
Gastric	Female/Male	All ages	N/A	USPSTF does not discuss
Hematologic	Female/Male	All ages	N/A	USPSTF does not discuss
Lung	Female/Male	50-80	B	Annual screening with LDCT for patients who currently smoke with history of smoking 20 packs of cigarettes/year or quit in past 15 years. Continue screening until patient has not smoked for 15 years or develops health complication that limits potential lung cancer intervention or life expectancy.
Oral	Female/Male	All ages	I	Insufficient evidence to recommend screening
Ovarian	Female	All ages	D	Recommend against screening in healthy individuals
Pancreatic	Female/Male	All ages	D	Recommend against screening in healthy individuals
Prostate	Male	55-69	C	Screening per patient status/preference
Prostate	Male	70 and older	D	Recommend against screening in healthy individuals
Skin	Female/Male	All ages	I	Insufficient evidence to recommend screening
Testicular	Female/Male	All ages	D	Recommend against screening in healthy individuals
Thyroid	Female/Male	All ages	D	Recommend against screening in healthy individuals

Abbreviations: USPSTF, United States Preventive Services Task Force; CT, computed tomography; FIT, fecal immunochemical test.

safest and most cost-effective medical tests available, but data to inform consistent guidelines are lacking.[19] The paucity of studies demonstrating mortality benefit and potential for sequelae of overdiagnosis led the USPSTF to conclude that evidence is insufficient [Grade I] to recommend for or against screening.[19] Alternatively, the ACS recommends periodic visual examination of the skin for general cancer prevention but does not specify frequency or age range.[19] Concerns over these guidelines include omission of disease morbidity and high-risk populations,[19] earlier detection of thinner melanomas with screening,[20] and overdiagnosis by primary care providers rather than experienced dermatologists.[21]

Table 2. United States Preventive Services Task Force Grade Definitions[1]

Grade	Definition	Suggestions for Practice
A	High certainty that the net benefit of screening is substantial	Offer this service
B	High to moderate certainty that the net benefit of screening is substantial	Offer this service
C	Moderate certainty that the net benefit of screening is small	Offer this service for select patients depending on professional judgement and patient preference
D	Moderate to high certainty that this service has no net benefit, or that the harms outweigh the benefit	Screening is discouraged
I	Evidence is insufficient to assess the balance of benefits and harms of this service	If the service is offered, patients should understand the uncertainty about the balance of harms and benefits

Some dermatologists suggest screening be considered for adults ages 35-75 who have at least 1 skin cancer risk factor.[19] Patients at highest risk are those with CDKN2A mutations, a personal history of skin cancer, greater than 100 common nevi, greater than 4 atypical nevi, indoor tanning use or excessive ultraviolet light exposure, fair skin, history of sunburns, geographic proximity to the equator, living at higher elevations, and weakened immune systems.[19] Organ transplant and immunocompromised patients also have a particularly increased burden with overall incidence and risk of invasive nonmelanoma skin cancer.[22] Though rare, it has been well documented that melanoma has associated paraneoplastic syndromes, including generalized melanosis[23] and dermatomyositis.[24] Additionally, adult-onset vitiligo has been reported both prior to and after the diagnosis of melanoma.[25]

Prostate Cancer Screening

The USPSTF states that prostate-specific antigen (PSA)-based screening is optional for males aged 55-69 years old [Grade C] and recommends against PSA-based screening in men 70 years

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and older [Grade D].[26] The association of prostatic malignancies with extramammary Paget's disease[27] and dermatomyositis[28] justifies screening beyond USPSTF recommendations. Since there is currently no consensus on prostate cancer screening guidelines for patients with extramammary Paget's disease and dermatomyositis, shared decision-making should incorporate known prostate cancer risk factors as well as risks and benefits of prostate cancer screening.[26]

Prostate cancer risk factors include older age, African American race, family history, BRCA1 and BRCA2 gene mutations, and Lynch syndrome.[26,29] PSA-based screening has a false-positive rate of approximately 1 in 6.[26] Transrectal ultrasound, MRI, and magnetic resonance spectroscopic imaging are less common screening modalities.[26] Other paraneoplastic dermatoses associated with prostate cancer include migratory thrombophlebitis, pityriasis rotunda, erythema gyratum repens, and acquired ichthyosis.[30]

Ovarian Cancer Screening

The USPSTF recommends against ovarian cancer screening in asymptomatic women [Grade D].[31] Screening is recommended for women with the following risk factors: personal or family history of breast cancer, BRCA gene mutation, pelvic inflammatory disease, endometriosis, ovarian cysts, Lynch syndrome, and smoking a pack of cigarettes daily for the past 20 years.[32] Though dermatological manifestations of ovarian cancer are uncommon, manifestations include dermatomyositis, acanthosis nigricans, secondary Raynaud's phenomenon, and palmar fasciitis with polyarthritis.[33] A complete pelvic exam, CA125 blood test, and transvaginal ultrasound are the recommended screening modalities for ovarian cancer.[34]

Hematologic Cancer Screening

Data is lacking for the USPSTF to offer screening recommendations for these cancers, but screening should be individually tailored to paraneoplastic dermatoses with well-established associations.[30] The strongest associations include paraneoplastic pemphigus with B-cell lymphoproliferative disorders; Sweet's syndrome and pyoderma gangrenosum with acute myelogenous leukemia; necrobiotic xanthogranuloma, POEMS syndrome, follicular hyperkeratotic spicules with plasma cell dyscrasias;[35,36] and acquired ichthyosis with Hodgkin's lymphoma.[30]

Pancreatic Cancer Screening

The USPSTF recommends against screening for pancreatic cancer in asymptomatic adults [Grade D] due to low incidence of disease and lack of available screening tests proven to reduce mortality or morbidity of disease.[37] For symptomatic individuals, CT with intravenous contrast is the preferred initial imaging modality,[38] along with blood tests and biopsy for definitive diagnosis.[39] For patients with suspected necrolytic migratory erythema, a serum glucagon level should be checked for glucagonoma diagnosis.[40] Additional cutaneous signs that have been reported with pancreatic cancer include migratory thrombophlebitis, hypertrichosis lanuginosa acquisita, palmar fasciitis and polyarthritis syndrome, dermatomyositis, pityriasis rotunda, palmoplantar keratoderma, and papular mucinosis.[41]

Thyroid Cancer Screening

The USPSTF recommends against screening for thyroid cancer in healthy asymptomatic adults [Grade D]. The task force found inadequate evidence to support the accuracy of neck palpation or ultrasound as a screening test. High-risk individuals (family history, inherited syndromes, history of radiation exposure to the head and neck) were not included in the review. For symptomatic individuals, ultrasound and fine-needle aspiration biopsy can detect thyroid cancer.[42]

Dermatologic manifestations of thyroid cancer are rare and usually occur from metastatic disease. New onset flesh-colored skin nodules, particularly in the scalp area, should raise clinical suspicion for metastatic thyroid carcinoma. While cutaneous metastasis predominantly occurs in patients with a known history of thyroid cancer, there are reports of such lesions leading to detection of occult thyroid cancer.[43]

Testicular Cancer Screening

Due to rare occurrence and favorable treatment outcomes of testicular cancer, the USPSTF recommends against routine testicular cancer screening in healthy adolescent or adult males [Grade D].[44] Clinical physical examination of the testicles may be indicated with the following risk factors: cryptorchidism, personal/family history of testicular cancer, HIV infection, Peutz-Jeghers syndrome, or carcinoma in situ of the testicles.[45] An ultrasound is recommended if clinical examination suggests testicular cancer.[44] There do not appear to be strong associations of paraneoplastic dermatoses with testicular cancer.[45]

Bladder Cancer Screening

The USPSTF does not recommend routine bladder cancer screening in healthy adolescents or adults [Grade I].[46] Screening may be indicated with the following risk factors: smoking, occupational carcinogen exposure, male sex, older age, White race, bladder parasitic infections, or personal/family history of bladder cancer.[46] Additionally, patients with extramammary Paget's disease or Muir-Torre syndrome should be screened for bladder cancer.[47] Urinalysis/cytology are the recommended screening tools as they are most efficient, noninvasive, and inexpensive.[47]

Oral and Gastric Cancer Screening

The USPSTF has determined that evidence is insufficient [Grade I] to provide guidelines for oral cancer screening,[48] though inspection and palpation of the oral cavity is reasonable for patients presenting with Bazex (acrokeratosis paraneoplastica) or Sweet's syndromes.[49] Similarly, there are no consensus statements for gastric cancer screening, but rare, yet strong associations exist with

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acanthosis nigricans—including tripe palms and Leser–Trélat.[30] Endoscopic workup for patients presenting acutely with these dermatoses may be warranted.[30]

CONCLUSIONS

Performing skin examinations is a crucial component of routine cancer screening because numerous skin conditions are associated with internal malignancies. Delays in accessing recommended malignancy screenings for paraneoplastic dermatoses can lead to more advanced and potentially metastatic/fatal disease. Pruritus without dermatitis ("itch without rash"), often described as a "paraneoplastic itch," is associated with several types of underlying solid and hematologic malignancies.[50] Patients with a suspected paraneoplastic dermatosis should obtain all age-appropriate cancer screenings and be referred to dermatology for any history, physical, or review of system concerns.

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