

# Test Your Knowledge:

## Ten Questions about Melanoma

This quiz is related to a Research article (10.1371/journal.pmed.0020265) and Perspective (DOI: 10.1371/journal.pmed.0020339) in the October issue of *PLoS Medicine*

Virginia Barbour

### Question 1. What is happening to the incidence of melanoma worldwide?

- It is increasing, especially among older men
- It is increasing, mostly in young people
- There is no change

### Question 2. Which of these statements best reflects what is known about survival nowadays after melanoma?

- Most people with melanoma will die of other causes
- Overall, five-year survival is around 40%
- Survival rates have not improved in the past 20 years

### Question 3. What is the evidence that sunscreen prevents melanoma?

- There have been several randomized controlled trials (RCTs) that show that sunscreen protects against melanoma
- Case control studies suggest that sunscreen protects against melanoma
- Systematic reviews show no conclusive evidence for or against protection from melanoma

### Question 4. Which one of the following statements best reflects opinion about clinically diagnosing malignant melanoma?

- There are no typical characteristics of melanoma
- Melanomas are always more pigmented than the surrounding skin
- A combination of shape, pigmentation, and regularity of shape and size can be used to help recognize melanoma clinically

### Question 5. Which of these statements best reflects the current opinion about population screening?

- There is good evidence that survival would improve if all high-risk groups were regularly screened
- If all the population was regularly checked for melanoma once every three years, most melanomas could be caught before metastatic spread
- There is no firm evidence that screening of the general population would have any effect on mortality

### Question 6. What is the most common site of melanoma in men?

- Back
- Scalp
- Limbs

### Question 7. The prognosis of malignant melanoma is determined predominantly by which of the following?

- The horizontal extent of the lesion
- Known genetic mutations present in the lesion
- A variety of factors including depth of invasion of the melanoma and presence in lymph nodes or spread

### Question 8. Which of these statements is most accurate about familial predisposition to melanoma?

- Most people with melanoma have an affected first-degree relative
- A family history of melanoma increases an individual's chance of getting melanoma, but most melanoma is sporadic
- A family history of red hair has no significant effect on risk of melanoma

### Question 9. Which of these statements best reflects the current evidence on how wide the margin should be around an excised thin (less than 2 mm, Breslow thickness) melanoma?

- 1–2 mm
- 1–2 cm
- At least 5 cm

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Virginia Barbour is a senior editor at *PLoS Medicine*. E-mail: vbarbour@plos.org

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**Question 10. Which of these statements best reflects the current evidence for the use of adjuvant treatment for metastatic melanoma?**

- Systematic reviews have shown that adjuvant chemotherapy is effective in improving survival in patients with metastatic melanoma
- There is no evidence that adjuvant treatment improves overall survival in people with metastatic melanoma
- Adjuvant therapy only works if given early after excision of the primary tumor

**Answer 1. It is increasing, especially among older men**

The incidence of melanoma is increasing. Since the mid-1960s, melanoma incidence has risen by 3%–8% per year, with greatest increases in elderly men [1]. One study from the United States that looked at incidence between 1986 and 2001 suggested that the 2.4-fold increase found was largely the result of increased diagnosis rather than increased incidence of disease [2].

**References**

1. Armstrong B (2004) Epidemiology of cutaneous melanoma and current trends. In: Thompson JF, Morton DL, Kroon BBR, editors. Textbook of melanoma. London: Martin Dunitz. pp. 65–80.
2. Welch HG, Woloshin S, Schwartz LM (2005) Skin biopsy rates and incidence of melanoma: Population based ecological study. *BMJ* 331: 481.

**Answer 2. Most people with melanoma will die of other causes**

Roughly 60% of those diagnosed with melanoma in the 1960s died of the disease compared with just 11% more recently, an improvement attributed mainly to early detection [1]. Survival is best for those with thin lesions and without lymph node involvement. Five-year survival for women with melanomas less than 1.5 mm wide is 97%; for men, it is 93% [2].

**References**

1. Beddingfield FC (2003) The melanoma epidemic: Res ipsa loquitur. *Oncologist* 8: 459–465.
2. MacKie RM, Bray CA, Hole DJ, Morris A, Nicolson M, et al. (2002) Incidence of and survival from malignant melanoma in Scotland: An epidemiological study. *Lancet* 360: 587–591.

**Answer 3. Systematic reviews show no conclusive evidence for or against protection from melanoma**

There is no conclusive evidence for the effect of sunscreen on melanoma; in particular, there have been no RCTs on this question. Systematic reviews of case control studies have shown no conclusive evidence about the effects of sunscreen use in preventing malignant melanoma. The most recent review in 2003 [1] included around 5,400 cases and about 7,600 controls, and found no significant difference in cases of melanoma between people who had “ever” used sunscreen and those who had “never” used sunscreen (odds ratio 1.0; 95% confidence interval, 0.8–1.2). One confounding issue is that people who use sunscreen probably spend more time in the sun. One RCT addressed this issue; it studied 87 people going on their summer holidays, and asked whether those who used sunscreen with a higher sun protection factor (SPF) spent more time in the sun than those who used sunscreen with a lower SPF. The RCT found that people using a higher SPF sunscreen spent significantly more time in the sun over the course of their holiday than those who used the lower SPF sunscreen [2].

**References**

1. Dennis LK, Beane Freeman LE, VanBeek MJ (2003) Sunscreen use and the risk of melanoma: A quantitative review. *Ann Intern Med* 139: 966–978.
2. Autier P, Dore JF, Negrier S, Lienard D, Panizzon R, et al. (1999) Sunscreen use and duration of sun exposure: A double-blind, randomized trial. *J Natl Cancer Inst* 91: 1304–1309.

**Answer 4. A combination of shape, pigmentation, and regularity of shape and size can be used to help recognize melanoma clinically**

Several characteristics are usually present in melanomas: asymmetry, border irregularity, color variegation, and diameter greater than 6 mm. These features form the basis of the so-called ABCD system of diagnosis [1]. However, this system has not been validated, and these characteristics also occur in some benign skin lesions, for example, seborrheic keratoses. A prospective study of 135 dermatologists assessed their opinions of 4,036 consecutive resected nevi and melanoma. The study found that those most skilled at the clinical detection of melanoma seem to unconsciously rely on cognitive processes, that is, the overall pattern compared to that of common nevi and comparative processes, that is, identifying the other nevi of an individual (the ugly duckling sign) rather than using the so-called ABCD algorithm [2].

**References**

1. Friedman RJ, Rigel DS, Kopf AW (1985) Early detection of malignant melanoma: The role of physician examination and self-examination of the skin. *CA Cancer J Clin* 35: 130–151.
2. Gachon J, Beaulieu P, Sei JF (2005) First prospective study of the recognition process of melanoma in dermatological practice. *Arch Dermatol* 141: 434–438.

**Answer 5. There is no firm evidence that screening of the general population would have any effect on mortality**

There are a number of markers for people at high risk of melanoma, including family history, presence of multiple nevi, previous skin cancer, immunosuppression, and sun sensitivity. Some guidelines do recommend increased surveillance in these groups [1]. However, there is no evidence from RCTs or systematic reviews that increased surveillance is effective in high-risk groups. There is no evidence that general population screening works. RCTs are underway to test such screening [2].

**References**

1. Ferrini RL, Perlman M, Hill L (1998) American College of Preventive Medicine practice policy statement: Skin protection from ultraviolet light exposure. *Am J Prev Med* 14: 83–86.
2. Aitken J, Elwood M (2004) Population screening for melanoma: Current evidence and a community based randomized trial. In: Thompson JF, Morton DL, Kroon BBR, editors. Textbook of melanoma. London: Martin Dunitz. pp. 100–114.

**Answer 6. Back**

Melanoma may occur on any skin surface, but the most common site for melanoma in men is on the back, whereas in women the most common site is on the legs [1].

**References**

1. Swerdlow AJ, dos Santos Silva I, Doll R (2001) Cancer incidence and mortality in England and Wales: Trends and risk factors. Oxford: Oxford University Press. 304 p.

**Answer 7. A variety of factors including depth of invasion of the melanoma and presence in lymph nodes or spread**

A new American Joint Committee on Cancer (AJCC) staging system for melanoma was introduced in 2002, and is now in international use [1]. It was derived using 17,600 patients from 13 melanoma treatment centers around the world.

For a stage I tumor (a tumor less than 2 mm thick with no ulceration or spread), survival is 85% at ten years; for a stage IV tumor (distant metastases present) survival is 6%.

#### References

1. Greene FL, Page DL, Fleming ID, Fritz A, Balch CM, editors (2002) AJCC staging manual, 6th ed. New York: Springer-Verlag. 484 p.

### Answer 8. A family history of melanoma increases an individual's chance of getting melanoma, but most melanoma is sporadic

The estimated genetic component for melanoma is 18% [1]. Any family history of melanoma increases relative risk for an individual of developing melanoma themselves by about three. If there is a strong family history of the disease (three or more first-degree relatives with the disease), relative risk increases to 37–70. A family history of red hair increases relative risk of melanoma by three to four. In fewer than 2% of cases, melanoma is due to the presence of identifiable, heritable mutations in particular genes [2]. Two identified genes are *CDKN2A* and, more rarely, *CDK4* [3].

#### References

1. Hemminki K, Lonnstedt I, Vaitinen P, Lichtenstein P (2001) Estimation of genetic and environmental components in colorectal and lung cancer and melanoma. *Genet Epidemiol* 20: 107–1161.
2. Goldstein AM, Tucker MA (1995) Genetic epidemiology of familial melanoma. *Dermatol Clin* 13: 605–612.
3. Kefford RF, Mann GJ (2003) Is there a role for genetic testing in patients with melanoma? *Curr Opin Oncol* 15: 157–161.

### Answer 9. 1–2 cm

For thin melanomas, two systematic reviews and two subsequent RCTs have shown no significant difference in overall survival over 4–10 years between wide excision (4–5 cm excision margins) and more limited surgery (1–2 cm excision margins) [1–4]. Although most RCTs did not look at harms, one found that wider excision increased the need for skin grafting and the duration of hospital stay compared with narrower excision [5]. No study has compared an excision margin of 1–2 cm versus 1–2 mm.

#### References

1. Lens MB, Dawes M, Goodacre T, Bishop JA (2002) Excision margins in the treatment of primary cutaneous melanoma: A systematic review of randomized controlled trials comparing narrow vs wide excision. *Arch Surg* 137: 1101–1105.
2. Haigh PI, DiFronzo LA, McCready DR (2003) Optimal excision margins for primary cutaneous melanoma: A systematic review and meta-analysis. *Can J Surg* 46: 419–426.
3. Khayat D, Rixe O, Martin G, Soubrane C, Banzet M, et al. (2003) Surgical margins in cutaneous melanoma (2 cm versus 5 cm for lesions measuring less than 2.1-mm thick). *Cancer* 97: 1941–1946.
4. Thomas JM, Newton-Bishop J, A'Hern R, Coombes G, Timmons M, et al. (2004) Excision margins in high-risk malignant melanoma. *N Engl J Med* 350: 757–766.
5. Balch CM, Urist MM, Karakousis CP, Smith TJ, Temple WJ, et al. (1993) Efficacy of 2-cm surgical margins for intermediate-thickness melanomas (1 to 4 mm): Results of a multi-institutional randomized surgical trial. *Ann Surg* 218: 262–267.

### Answer 10. There is no evidence that adjuvant treatment improves overall survival in people with metastatic melanoma

A Cochrane review in 2000 of adjuvant treatment for metastatic melanoma found no evidence from randomized

controlled clinical trials to show any advantage of systemic therapy over best supportive care/placebo in the treatment of metastatic cutaneous malignant melanoma [1].

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1. Crosby T, Fish R, Coles B, Mason MD (2000) Systemic treatments for metastatic cutaneous melanoma. *Cochrane Database Syst Rev* 2: CD001215.

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