0117. People with Sickle Cell Deserve More Respect from Health Care Providers 镰状细胞患者应该得到医护人员的更多尊重

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1. People with Sickle 镰刀 Cell Deserve (v.) More Respect from Health Care Providers 镰状细胞患者应该得到医疗保健提供者的更多尊重

Example 1. title
sickle

New CRISPR-based treatments for *sickle cell disease* bring hope, but medical providers (n.) still **marginalize** (v.)使显得微不足道；使处于边缘；使无实权 people with this condition **far too often**.

When I first started my career in emergency medicine 急诊医学 28 years ago, the main treatments for this disease were intravenous (a.)注入静脉的；静脉内 fluids (液体；流体)静脉输液, oxygen and a powerful narcotic (n.)麻醉性镇痛药；镇静剂；麻醉药 used to manage the pain of sickle cell. The people with sickle cell, who are mostly Black, are often marginalized in many ways, including in health care.

基于CRISPR的镰状细胞病新疗法带来了希望，但医疗服务提供者仍然经常将患有这种疾病的人边缘化.
28年前，当我第一次开始从事急诊医学工作时，这种疾病的主要治疗方法是静脉输液、氧气和一种用于控制镰状细胞疼痛的强效麻醉剂。 镰状细胞病患者大多是黑人，他们往往在许多方面被边缘化，包括在医疗保健方面。

Sickle cell is caused by *an autosomal 常染色体的 recessive 隐性的 mutation* （生物物种的）变异，突变 on one of the chromosomes we inherit (v.) from our parents, meaning that /in order for 为了达到某个结果或目的 someone to have the condition, they have to inherit (v.) this mutated 突变 gene from both of their parents. Sickle cell disease is caused by what's called a point mutation 点突变 — a change at a single spot 地点 on our DNA — that damages (v.) normal hemoglobin 血红蛋白, the protein that helps (v.) blood carry (v.) oxygen through our body.

镰状细胞是由我们从父母那里继承的一条染色体上的常染色体"隐性突变"引起的，这意味着为了让某人患有这种疾病，他们必须从父母双方那里都继承这种突变基因。 镰状细胞病是由所谓的"点突变"引起的，即我们DNA上单个点的变化，会损害正常的血红蛋白，血红蛋白是"帮助血液将氧气输送到我们身体"的蛋白质。

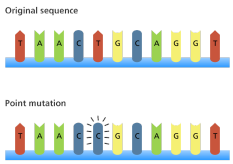
Example 2. title

recessive

-→ 来自 recess,后退，-ive,形容词后缀。引申词义隐性的。

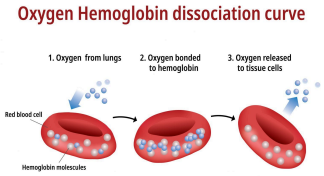
point mutation

点突变：一种基因突变，涉及到单个核苷酸碱基的替代、添加或删除。
"点突变"指只有一个"碱基对"发生改变。广义"点突变"可以是碱基替换，单碱基插入, 或碱基缺失；狭义"点突变"也称作"单碱基替换"（base substitution）。碱基替换又分为转换（transitions）和颠换（transversions）两类。"点突变"具有很高的回复突变率。



hemoglobin

-→ 来自古希腊语αἷμα("blood") + 拉丁语globus("ball, sphere") + -in.

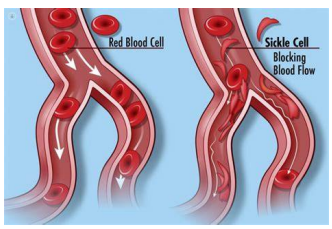


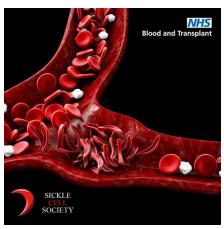
Those misshapen hemoglobin proteins stick (v.) 粘贴；粘住 together in people with sickle cell, distorting (v.) 使变形；扭曲；使失真 the shape of red blood cells from a round shape to a sickle one that cannot flow (v.) through our blood vessels as easily. The blood cells get “stuck” to one another and block the vessels in the bones, spleen 脾 and various organs as they try to traverse (v.)横过；横越；穿过；横渡 through the body. When the cells of people with sickle cell clog (v.)（使）阻塞，堵塞 their blood vessels, they are in extreme pain that can last (v.) for several days as their body **figures out** 找到答案，解决;弄清楚，弄明白 how to clear the blockage 造成阻塞的东西；阻塞物. We call this a crisis.

这些畸形的血红蛋白, 在镰状细胞患者中粘在一起，使红细胞的形状从圆形扭曲为镰状，不能轻易流过我们的血管。血细胞相互“粘附”，阻塞骨骼、脾脏和各种器官的血管，因为它们试图穿过身体。 当镰状细胞患者的细胞堵塞血管时，他们会处于极度疼痛中，这种疼痛可能会持续数天，因为他们的身体会弄清楚如何清除阻塞。 我们称之为危机。

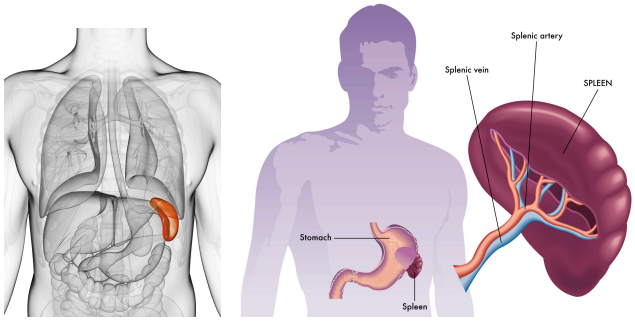
Example 3. title

sickle cell





spleen



traverse

(v.) [VN] (technical 术语) /trəˈvɜːs/ (formal) to cross an area of land or water 横过；横越；穿过；横渡
-→ tra-横过,越过 + -vers-转 + -e动词词尾

In high-stress conditions, such as infection, heat, dehydration 脱水 or even mental duress (n.)胁迫；强迫, where oxygen is low, the sickling （使）变成镰状细胞 gets worse. The blood cells of people with sickle cell die (v.) prematurely (ad.)过早地. As a result, these individuals suffer (v.) from complications 并发症 that are normally seen in people who are much older, and they have a much shorter life expectancy than people without sickle cell.

在高压力条件下，例如感染、高温、脱水甚至精神胁迫，氧气含量低，镰状细胞会变得更糟。 镰状细胞患者的血细胞, 会过早死亡。 因此，这些人患有"通常在年龄大得多的人身上看到的"并发症，而且他们的预期寿命, 比没有镰状细胞的人短得多。

Example 4. title

duress

(n.)[U] (formal) threats or force that are used to make sb do sth 胁迫；强迫
→ 来自拉丁语durus, 硬，词源同endure, tree.引申义强硬，胁迫。
- He signed (v.) the confession under duress . 他出于被迫在供状上签了字。

When both parents have the genetic trait （人的个性的）特征，特点；遗传特征 for sickle cell, there is a 50 percent chance they will have a child who has the trait but does not typically have symptoms of the disease /and a 25 percent chance that they will have a child with sickle cell disease with each pregnancy. The chance of having a child with sickle cell disease jumps (v.) to 50 percent /if one parent has the disease itself and the other parent has the trait.

当父母双方都具有"镰状细胞"的遗传性状时，他们有50%的几率, 会生出"具有该性状, 但通常没有疾病症状的"孩子. 并且有25%的几率, 在每次怀孕时, 生出患有"镰状细胞病"的孩子。 如果父母一方患有镰状细胞病，而另一方带有镰状细胞性状时，则孩子患有镰状细胞病的几率跃升至50%。

I have seen countless adults with sickle cell **come in** with pain related to crises 危机，紧要关头；危险期 and other complications that occur (v.) /原因状 as the disease continues to take a toll 造成重大损失（或伤亡、灾难等） on their prematurely 过早地 aging (a.) body.

As time passes, I have seen them go **from** functional (a.)（能）起作用的，工作的，运转的 **to** frail (a.)瘦弱的;弱的；易损的；易碎的 — suffering from the multiple complications of the disease, including *arthritic 患关节炎的；关节炎引起的* *joints* 关节炎, *blood clots* （（血或乳脂）凝结成块) 血栓,血凝块, severe infections and strokes. I always worry about whether they are dead or alive /when there is a long period of time in which I haven't seen them.

我见过无数患有镰状细胞的成年人, 因危机和其他并发症, 而感到疼痛，因为这种疾病继续对他们过早衰老的身体造成伤害。
/我见过无数患有镰状细胞的成年人，他们的身体过早衰老，由于疾病继续对他们造成伤害，他们的身体出现了与危机和其他并发症相关的疼痛。
随着时间的流逝，我看到他们从功能性到虚弱——**患有这种疾病的多种并发症，包括关节炎、血栓、严重感染和中风。** 我总是担心他们是死是活，因为我有很长一段时间没有见过他们。

Example 5. title

. chatGPT : 这句话中的 "come in" 意思是指患有镰状细胞病的成年人, 经常因为危机引起的疼痛和疾病并发症, 而就医或入院。

take a heavy 'toll (on sb/sth) } take its 'toll (on sb/sth)

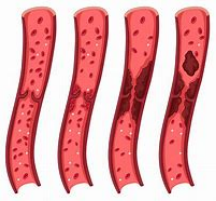
to have a bad effect on sb/sth; to cause a lot of damage, deaths, suffering, etc. 产生恶果；造成重大损失（或伤亡、灾难等）
• Illness had taken a heavy toll on her. 疾病对她的身体造成极大的损害。

toll
（战争、灾难等造成的）毁坏；伤亡人数
-→ 来自古英语 toll,费用，税费，关税，来自 Proto-Germanictullo,计算数，告知，来自 PIEdol, 计算，思考，词源同 tell,tall.引申诸相关词义。

frail

(a.)1.(especially of an old person 尤指老人) physically weak and thin 瘦弱的
2.weak; easily damaged or broken 弱的；易损的；易碎的
缩写自拉丁语fragilis, 易碎的，词源同fragile.

blood clots



And over the years, I have seen the number of “regulars” 常客；老主顾 I have known diminish (v.)减少；（使）减弱，缩减；降低 as they have fallen to their ultimate 最后的；最终的；终极的 and unavoidable end — death at a median age of 53 years. These individuals’ chance of early mortality (死亡)早逝 is even higher if they are male or happen to have been born in sub-Saharan Africa, where up to 90 percent of children with the disease will die during childhood, usually before their fifth birthday.

多年来，我看到我认识的“常客”数量减少，因为**他们已经跌落到最终和不可避免的结局——在中位年龄 53 岁时死亡。**如果这些人是男性或碰巧出生在撒哈拉以南非洲，那么他们过早死亡的几率甚至更高，那里高达90%的患有这种疾病的儿童将在童年时期死亡，通常在他们五岁生日之前。

There are few therapies 治疗方法 for people with sickle cell. Parents, who often do not know their own status as a carrier, would be given genetic counseling /if it was available. If they proceeded 继续做（或从事、进行） to have a child with the disease, they would have to prepare for a lifetime of stress and high costs **attributable (a.)可归因于；可能由于 to** a condition marked 赋予特征；给…确定性质 by periods of agonizing (a.)使人十分痛苦的；令人焦虑不安的；带来巨大困难的 pain, repeated hospitalizations 住院治疗；医院收容 and early death.

主 Individuals living with this condition 谓 pay (v.) four times *the out-of-pocket 需现款支付的 costs* of those without it, with insurers 保险公司 paying (v.) approximately $1.7 million per person for medical services **attributable (a.)可归因于；可能由于 to** the illness.

镰状细胞患者的治疗方法很少。父母通常不知道自己作为携带者的身份，如果有的话，将接受遗传咨询。 如果他们继续生下**患有这种疾病的孩子，他们将不得不为一生的压力和高昂的费用做好准备，这些压力和高昂的费用是以痛苦的疼痛、反复住院和早逝为特征的疾病。**
患有这种疾病的人支付的自付费用, 是没有这种疾病的人的四倍，保险公司为每人支付约170万美元的医疗服务费用。

So, it’s good news that the FDA has approved two cell-based therapies for sickle cell disease — Casgevy and Lyfgenia. These are the first gene therapies for sickle cell disease based on the CRISPR/Cas9 technology. This technology, the development of which won (v.) a Nobel Prize in 2020, enables an individual’s DNA to be changed with “genetic scissors 剪刀.” In the case of 关于；就…而言；在…情况下 sickle cell, this change promotes (v.) production of fetal

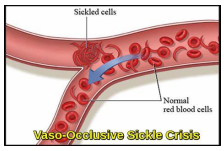
胎儿的 hemoglobin 血红蛋白, which takes the place of 取代（某人或某物） the mutated hemoglobin 血红蛋白, reducing the number of cells that sickle (a.)镰刀型的. This lowers (v.)减少; 降低 the chance of one of the most painful crises (n.)危机 experienced by patients with sickle cell: the vaso-occlusive (a.)血管闭塞性的, or blocked blood vessel, crisis 危机. The treatment also increases life expectancy.

因此，好消息是FDA已经批准了两种基于细胞的镰状细胞病疗法——Casgevy和Lyfgenia。 这是第一个**基于CRISPR / Cas9技术的镰状细胞病基因疗法。** 这项技术的开发获得了2020年的诺贝尔奖，**它能够用"基因剪刀"改变一个人的DNA。**在镰状细胞的情况下，这种变化促进了胎儿血红蛋白的产生，胎儿血红蛋白取代了突变的血红蛋白，减少了镰状细胞的数量。 **这降低了镰状细胞患者经历的最痛苦的危象之一的几率：血管闭塞或血管阻塞危象。**这种治疗还可以延长预期寿命。

Example 6. title
occlusive

ADJ of or relating to the act of occlusion 闭合的

vaso-occlusive



Prior (a.) to 在前面的 this therapy, curative 能治病的；有疗效的 options were limited to bone 骨头；骨 marrow 精华; 精髓; 核心 transplants from donors, which were prohibitive 高昂得令人难以承受的；贵得买不起的 because a person with sickle cell would need a matched donor 捐赠者；捐赠机构 but also because of the risk of mortality linked to rejection （对移植器官的）排斥.
在这种疗法之前，治疗选择仅限于来自供体的骨髓移植，这是令人望而却步的，因为镰状细胞患者需要匹配的供体，但也因为与排斥反应相关的死亡风险。

Funding for research for sickle cell disease is significantly less than the funding for other inheritable 可遗传的；有遗传性的 childhood diseases. For example, over a 10-year period, the National Institutes of Health has funded sickle cell disease research at an amount /equivalent to $812 *per affected person*. Private funding is minuscule (a.)极小的；微小的 at $102 *per affected person*.

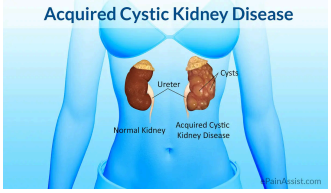
镰状细胞病研究的资金, 明显少于其他遗传性儿童疾病的资金。 例如，在10年的时间里，美国国立卫生研究院（National Institutes of Health）资助了镰状细胞病研究，金额相当于每个受影响的人812美元。 私人资金微乎其微，每人102美元。

Contrast (v.)对比；对照 this with *cystic 胞囊的; 膀胱的; 胆囊的 fibrosis* [医] 纤维化, which affects 30,000 people in the U.S., compared with the 90,000 people affected by sickle cell disease. Over those same 10 years, the NIH funded $2,807 of research per person affected by *cystic fibrosis* 囊性纤维化, and private organizations have funded $7,690 per person with the condition.

与此形成鲜明对比的是囊性纤维化，囊性纤维化影响了美国30,000人，而受镰状细胞病影响的人为90,000人。 在这10年中，美国国立卫生研究院资助了每位"囊性纤维化"患者2,807美元的研究，私人组织资助了每位患有囊性纤维化的人7,690美元。

Example 7. title
cystic

ADJ of, relating to, or resembling a cyst 胞囊的; 膀胱的; 胆囊的
1.MEDICINE relating to or characterized by cysts.
- the ultrasound scan showed a cystic nodule 小结；小瘤；节"
2.relating to the urinary bladder or the gall bladder.
- the cystic artery 动脉



cystic fibrosis

[U] a serious medical condition that some people are born with, in which glands 腺体 in the lungs and other organs do not work correctly. It often leads to infections and can result in early death. 囊性纤维变性；囊性纤维化

囊性纤维化：一种常见的进行性遗传疾病，通常在婴儿期或幼儿期出现，**其特点是黏液在各种器官的导管和通道中积聚，尤其是在肺和胰腺中，导致呼吸困难、持续咳嗽、慢性呼吸道感染**、胰腺酶不足、消化功能障碍、营养不良和生长迟缓。

Is it any wonder, then, that few new therapies have emerged for sickle cell disease?

那么，难怪很少有针对镰状细胞病的新疗法出现呢？

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2. People with Sickle Cell Deserve More Respect from Health Care Providers

New CRISPR-based treatments for sickle cell disease bring hope, but medical providers still marginalize people with this condition far too often

When I first started my career in emergency medicine 28 years ago, the main treatments for this disease were intravenous fluids, oxygen and a powerful narcotic used to manage the pain of sickle cell.

the people with sickle cell, who are mostly Black, are often marginalized in many ways, including in health care.

Sickle cell is caused by an autosomal recessive mutation on one of the chromosomes we inherit from our parents, meaning that in order for someone to have the condition, they have to inherit this mutated gene from both of their parents.

Sickle cell disease is caused by what's called a point mutation—a change at a single spot on our DNA—that damages normal hemoglobin, the protein that helps blood carry oxygen through our body. Those misshapen hemoglobin proteins stick together in people with sickle cell, distorting the shape of red blood cells from a round shape to a sickle one that cannot flow through our blood vessels as easily. The blood cells get "stuck" to one another and block the vessels in the bones, spleen and various organs as they try to traverse through the body. When the cells of people with sickle cell clog their blood vessels, they are in extreme pain that can last for several days as their body figures out how to clear the blockage. We call this a crisis.

In high-stress conditions, such as infection, heat, dehydration or even mental duress, where oxygen is low, the sickling gets worse. The blood cells of people with sickle cell die prematurely. As a result, these individuals suffer from complications that are normally seen in people who are much older, and they have a much shorter life expectancy than people without sickle cell. When both parents have the genetic trait for sickle cell, there is a 50 percent chance they will have a child who has the trait but does not typically have symptoms of the disease and a 25 percent chance that they will have a child with sickle cell

disease with each pregnancy. The chance of having a child with sickle cell disease jumps to 50 percent if one parent has the disease itself and the other parent has the trait.

I have seen countless adults with sickle cell come in with pain related to crises and other complications that occur as the disease continues to take a toll on their prematurely aging body.

As time passes, I have seen them go from functional to frail—suffering from the multiple complications of the disease, including arthritic joints, blood clots, severe infections and strokes.

I always worry about whether they are dead or alive when there is a long period of time in which I haven't seen them. And over the years, I have seen the number of "regulars" I have known diminish as they have fallen to their ultimate and unavoidable end—death at a median age of 53 years.

These individuals' chance of early mortality is even higher if they are male or happen to have been born in sub-Saharan Africa, where up to 90 percent of children with the disease will die during childhood, usually before their fifth birthday.

There are few therapies for people with sickle cell. Parents, who often do not know their own status as a carrier, would be given genetic counseling if it was available. If they proceeded to have a child with the disease, they would have to prepare for a lifetime of stress and high costs attributable to a condition marked by periods of agonizing pain, repeated hospitalizations and early death. Individuals living with this condition pay four times the out-of-pocket costs of those without it, with insurers paying approximately $1.7 million per person for medical services attributable to the illness.

So, it's good news that the FDA has approved two cell-based therapies for sickle cell disease—Casgevy and Lyfgenia. These are the first gene therapies for sickle cell disease based on the CRISPR/Cas9 technology. This technology, the development of which won a Nobel Prize in 2020, enables an individual's DNA to be changed with "genetic scissors." In the case of sickle cell, this change promotes production of fetal hemoglobin, which takes the place of the mutated hemoglobin, reducing the number of cells that sickle. This lowers the chance of one of the most painful crises experienced by patients with sickle cell: the vaso-occlusive, or blocked blood vessel, crisis. The treatment also increases life expectancy.

Prior to this therapy, curative options were limited to bone marrow transplants from donors, which were prohibitive because a person with sickle cell would need a matched donor but also because of the risk of mortality linked to rejection.

Funding for research for sickle cell disease is significantly less than the funding for other inheritable childhood diseases. For example, over a 10-year period, the National Institutes of Health has funded sickle cell disease research at an amount equivalent to $812 per affected person. Private funding is minuscule at $102 per affected person. Contrast this with cystic fibrosis, which affects 30,000 people in the U.S., compared with the 90,000 people affected by sickle cell disease. Over those same 10 years, the NIH funded $2,807 of research per person affected by cystic fibrosis, and private organizations have funded $7,690 per person with the condition. Is it any wonder, then, that few new therapies have emerged for sickle cell disease?