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PRESENTACION DE DIAPOSITIVAS VITAL

"MEASLES CASE MANAGEMENT AND VITAMIN A"

Too many infants and young children die from the complications of measles each year. Today, measles deaths can be prevented. The purpose of this slide presentation is to update health professionals on measles case management including a new way of reducing measles complications and mortality by giving oral vitamin A supplements. The slides can be used as part of a formal training course or an informal refresher/orientation session for health professionals and para-professionals. The presentation contains an overview of all the essential elements of case management. It emphasizes newer aspects such as vitamin A supplementation, including the results of studies in which the association of vitamin A and measles was identified and the effect of treatment tested. It also provides practical guidance on topics such as diagnosing complications, supplies needed at health centers, doses for different age groups, vitamin A preparations and how to administer them.

"CAUSES OF CHILD MORTALITY"

Despite the availability of a highly effective vaccine, measles is still responsible for more deaths than all other EPI (Expanded Program of Immunization) target diseases combined. In developing countries, measles case fatality rates are 20 times those currently reported in developed countries. Community studies of measles outbreaks between 1961 and 1990 show case fatality rates from 1.5 to 30 percent. High measles mortality was initially thought to occur only in Africa, but high rates have now been reported in Asia and Latin America as well. Important reasons for the high mortality seen in developing countries include: young age at the time of infection, poverty, overcrowding and intensity of exposure, and absent or delayed medical care. Nutritional status, especially vitamin A status, has been recognized as a critical factor in recent years.

"MEASLES OUTCOMES"

Deaths from measles occur mainly due to complications such as pneumonia, diarrhea and croup. Other complications of measles namely, blindness, otitis media, encephalitis and growth failure result in lifelong disabilities. The incidence of illness and death (from other childhood illnesses) in the months following an outbreak of measles can be ten times greater in measles survivors. Thus, not only does measles cause death and complications in the acute phase, but the longer term effects of an attack of measles can also be seen in the reduced survival rates of infected infants and young children over a period of many months. Those who survive the acute disease have a greatly increased chance of dying from a variety of other conditions, compared with those not infected with measles. The younger the age at the time of infection, the more noticeable is this delayed mortality phenomenon.

"IMPACT OF VITAMIN A"

SLIDE 4

Half of all blindness in Africa is attributed to measles. Studies in Asia and Africa reported that low vitamin A blood levels were associated with measles and that low vitamin A blood levels increased the risk of death in children. Low blood levels in measles patients were reported not only in areas where vitamin A deficiency was a serious problem, but also in areas where clinical signs of vitamin A deficiency were not commonly seen. Recently, three randomized clinical trials with vitamin A supplements showed conclusively that treatment of severe cases of measles with at least two doses of 200,000 IU of oral vitamin A reduced the severity and duration of complications and reduced mortality

— POINT TO GRAPH —

WHO has issued directives on routinely giving oral vitamin A supplements to children with severe measles.

"MEASLES AND VITAMIN A"

SLIDE 5

— READ FROM SLIDE —

"CASE MANAGEMENT"

SLIDE 6

— READ FROM SLIDE —

"IS IT MEASLES?"

SLIDE 7

The first step in case management is accurate and timely identification of all cases. Measles can be diagnosed as shown here.

— READ FROM SLIDE —

In summary, the simple clinical case definition for diagnosing measles is: fever for more than three days with a characteristic rash, and at least one of the following — cough, runny nose, red eyes.

"VITAMIN A SCHEDULE"

The vitamin A protocol for measles is shown here. According to published studies the dosage recommended here is absorbed sufficiently to have an impact, even though diarrhea is often present with the measles. Infants under 12 months of age and those weighing less than 8 kilos, receive half the dose, equalling 100,000 IU instead of 200,000 IU.

"DOSING WITH VITAMIN A"

Vitamin A is available in capsules or in a liquid concentrate. Older children can swallow a capsule that contains 200,000 IU. However, children under 2 years of age will need to have the contents squeezed out into their mouths. The number of drops in a capsule of vitamin A may vary from 6-8 drops. When each new batch of capsules is unpacked, measure the number of drops by cutting open a capsule and measuring its contents in drops. The full contents of each capsule equal one dose of 200,000 IU. For infants under 12 months, cut open the capsule and squeeze out half the number of drops directly into the their mouth. This equals one dose of 100,000 IU. Children too sick to swallow a capsule can be given the supplement in this way also.

"VITAMIN A SUPPLIES"

Vitamin A supplementation of measles cases can be readily adapted to fit into many primary health care programs because it has a number of advantages: it can be easily given by mouth and no injections are needed, the supplement requires no refrigeration, and has a reasonably long shelf life — 2 years in an unopened bottle and 6 months once the bottle has been opened.

— READ FROM SLIDE —

"FEEDING AND FLUIDS ARE CRITICAL"

Feeding of the child with measles, and teaching the child's caretaker at home about special feeding, are key elements for all patients. A critical factor that was noted in several of the clinical studies on measles complications was the extent to which young children lost weight and how frequently clinical signs of protein-calorie malnutrition appeared in measles survivors. The lowered resistance to diarrhea, pneumonia and other diseases following measles can continue for up to one year and can be attributed at least in part to protein-calorie malnutrition from which these children may never recover, unless special measures are taken to actively increase weight gain following the initial measles episode. Mothers and other family members should not stop feeding the child with measles. If possible, the amount and frequency of feedings should be increased using high calorie and nutrient-rich foods. The child's weight gain should be monitored frequently. To motivate the child's care-giver to provide

continued care to the measles survivor in the home, it should be clearly pointed out that the risk of dying does not pass as quickly as the disappearance of rash and fever in measles.

"NUTRITION MESSAGES"

— READ FROM SLIDE —

Explain to the mother/caregiver that measles has severely weakened the child. Remind her to give more food more often. If diarrhea is present, give more fluids. Special foods or expensive supplements are generally not necessary for children recuperating from measles. Traditional foods, prepared with locally popular weaning dishes can be enriched by adding ingredients rich in energy, protein, vitamins and minerals. Mothers or caretakers will need to be shown the types and quantities of desired foods for younger children. Children should be monitored for weight weekly or monthly.

"COMPLICATIONS"

The child with measles should be screened and kept under observation for complications. Prompt treatment is the key to saving lives. WHO has issued guidelines for treating complications for some conditions including diarrhea and respiratory infections. We will briefly review some of the important points.

— READ FROM SLIDE —

"PNEUMONIA"

— READ FROM SLIDE —

"EYE LESIONS"

— READ FROM SLIDE —

"DIARRHEA/DEHYDRATION"

— READ FROM SLIDE —

"SUPPLIES NEEDED"

— READ FROM SLIDE —

"IMMUNIZATION"

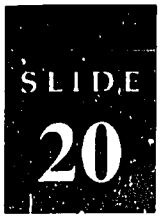
As we begin to devote new resources to improving measles case management, we should not forget that prevention is better than cure. In fact, the primary intervention for effective and sustained measles control is universal immunization. The single most important determinant of measles morbidity and mortality is vaccination status. Universal immunization is the permanent solution to measles. Yet coverage remains well below 100 per cent.

"EXPANDING COVERAGE"

Greater efforts are needed to increase coverage. This is a summary of key principles.

— READ FROM SLIDE —

"TARGETS FOR 1995"



Measles has claimed over 3 million lives of children during the past two years. In addition to these deaths, children who survived the initial infection have experienced an incidence of illness and death that is ten times greater than children who did not have measles. Thus UNICEF has called measles "one of the single most deadly threats to the children of the 1990's." Recent research shows that there is hope for the child who contracts measles — vitamin A dosing of measles cases and the prompt treatment of complications must become universal practices. It is essential also to train mothers in nutritional recuperation of the child with a history of measles because these children remain at high risk of morbidity and mortality for up to one year after infection. The strategy that has been described in this slide presentation can go a long way in meeting targets for 1995 set at the World Summit for Children held in 1990.

— READ QUOTE FROM SLIDE —

In summary, a comprehensive measles control strategy should include both — effective case management and prevention through immunization.

— READ "STRATEGY" FROM SLIDE —

"PRISE EN CHARGE DE LA ROUGEOLE ET DE LA VITAMINE A"

1

Bien trop de nourrissons et de jeunes enfants meurent des conséquences de la rougeole chaque année. Dans une communauté asiatique, chaque mort causée par la rougeole est suivie par une offrande, sous forme de figure en bois, à la déesse de la rougeole "mata."

— MONTRER LA DIAPOSITIVE —

Aujourd'hui, nous pouvons prévenir la mortalité causée par la rougeole. Ce diaporama vise à communiquer aux professionnels de la santé les informations les plus récentes sur le traitement de la rougeole, y compris sur les nouvelles modalités de réduction des complications et de la mortalité grâce à l'administration de compléments vitaminiques A oraux. Ces diapositives peuvent être utilisées dans le cadre d'un stage de formation officiel ou servir de support informel pour des séances de mise à jour/orientation à l'intention de professionnels et para-professionnels de la santé. La présentation donne une vue d'ensemble de tous les éléments essentiels du traitement de la rougeole en mettant l'accent sur les aspects les plus récents tels que l'administration de compléments vitaminiques, avec notamment les résultats d'études qui ont révélé les rapports entre la vitamine A et la rougeole et testé les effets des traitements. Ce diaporama donne en outre une orientation pratique dans des domaines tels que le diagnostic des complications, les médicaments dont doit disposer un centre de santé, les doses à administrer à différents groupes d'âge et les préparations et modalités d'administration de vitamine A.

"CAUSES DE LA MORTALITE JUVENILE"

2

En dépit de l'existence d'un vaccin fort efficace, la rougeole continue de provoquer plus de morts que toutes les autres maladies visées par le PEV (Programme élargi de vaccination) combinées. Dans les pays en développement, le taux de mortalité attribuable à la rougeole est 20 fois supérieurs à celui signalé dans les pays industrialisés. Les études en milieu communautaire réalisées sur les poussées de rougeole entre 1961 et 1990 révèlent du taux de mortalité de 1,5 à 30 %. On pensait initialement que le taux élevé de mortalité ne se produisaient qu'en Afrique, mais des chiffres particulièrement élevés ont également été signalés en Asie et en Amérique latine. Parmi les principales causes de ce phénomène dans les pays en développement, on citera : infection des jeunes, pauvreté, surpeuplement et intensité de l'exposition et soins médicaux inexistants ou insuffisants. Durant ces dernières années, on a reconnu le caractère crucial de l'état nutritionnel, et tout particulièrement celui de la vitamine A.

"CONSEQUENCES DE LA ROUGEOLE"

La mortalité due à la rougeole est principalement attribuable aux complications telles que la pneumonie, la diarrhée et le croup. Il est d'autres complications telles que la cécité, l'antrite, l'encéphalite et les troubles de croissance qui provoquent des incapacités à vie. L'incidence de la maladie et de la mortalité (causée par d'autres maladies de l'enfance) durant les mois qui suivent l'apparition de la rougeole peut être dix fois plus élevée chez les personnes qui ont survécu à la rougeole. Autrement dit, la rougeole est cause de mortalité et de complications durant la phase aiguë, et qui plus est, la maladie a des effets à plus long terme qui se traduisent par des taux de survie réduits chez les nourrissons et les jeunes enfants infectés pendant plusieurs mois. Ceux qui survivent la phase aiguë de la maladie courent plus de risques de mourir d'une série d'autres maux que les sujets n'ayant pas été infectés par la rougeole. Plus le sujet infecté est jeune et plus ce phénomène de mortalité retardée est notable.

"EFFET DE LA VITAMINE A"

La moitié des cas de cécité en Afrique sont attribuables à la rougeole. Des études entreprises en Afrique et en Asie signalent qu'un rapport a pu être établi entre de faibles niveaux de vitamine A dans le sang et la rougeole, et que ces faibles niveaux provoquaient un accroissement du risque de mortalité chez les enfants. Ces faibles niveaux chez les patients souffrant de rougeole étaient signalés non seulement dans les régions où les carences vitaminiques A posaient un grave problème mais également là où les signes cliniques des carences vitaminiques A n'étaient pas couramment observés. Dernièrement, trois essais cliniques aléatoires avec compléments de vitamine A ont clairement établi que le traitement des cas graves de rougeole avec au moins deux doses de 200 000 IU de vitamine A orale réduisait la gravité et la durée des complications ainsi que la mortalité.

-- MONTRER GRAPHIQUE —

L'OMS a publié des directives pour l'administration courante de compléments vitaminiques A aux enfants souffrant de rougeole aiguë.

"LA ROUGEOLE ET LA VITAMINE A"

— LIRE LA DIAPOSITIVE —

"INTERVENTIONS"

6

— LIRE LA DIAPOSITIVE —

"EST-CE LA ROUGEOLE ?"

7

La première étape de toute intervention consiste à dépister correctement et à temps tous les cas. Le diagnostic de la rougeole peut être établi comme suit.

— LIRE LA DIAPOSITIVE —

En résumé, la définition clinique simple du diagnostic de la rougeole est la suivante : fièvre pendant plus de trois jours avec une éruption caractéristique et au moins un des symptômes suivants : toux, nez qui coule, yeux rouges.

"QUAND ET COMMENT ADMINISTRER LA VITAMINE A ?"

8

Cette diapositive indique le protocole d'administration de vitamine A dans les cas de rougeole. Selon les études publiées, le dosage qui est ici recommandé est suffisamment absorbé pour produire un effet, et ce en dépit de la diarrhée qui accompagne souvent la rougeole. Les enfants de moins de 12 mois, et ceux qui pèsent moins de 8 kilos doivent recevoir la moitié, soit 100 000 IU au lieu de 200 000 IU.

"LE DOSAGE DE LA VITAMINE A"

9

La vitamine A existe en capsules ou sous forme de concentré liquide. Les enfants plus âgés peuvent avaler une capsule contenant 200 000 IU. Par contre, les enfants de moins de 2 ans ne peuvent pas avaler la capsule, mais seulement son contenu. Le nombre de gouttes dans une capsule de vitamine A varie de 6 à 8. Chaque fois qu'un nouveau lot de capsules est ouvert, il convient de compter le nombre de gouttes en ouvrant une des capsules. Le contenu de chaque capsule équivaut à une dose de 200 000 IU. Dans le cas des jeunes enfants de moins de 12 mois, ouvrir la capsule et leur faire avaler directement la moitié du contenu. Cela équivaut à une dose de 100 000 IU. On peut également administrer la vitamine A de la sorte aux enfants qui sont trop malades pour avaler une capsule.

"L'APPROVISIONNEMENT EN VITAMINE A"

10

La vitamine A dans les cas de rougeole peut aisément s'adapter pour s'inscrire dans n'importe quel programme de soins de santé primaires car elle présente un certain nombre d'avantages : elle peut être aisément administrée par voie orale et aucune injection n'est nécessaire, les compléments n'exigent pas de refroidissement et leur durée de vie est relativement longue (deux ans pour un flacon non entamé et 6 mois lorsqu'il est entamé).

— LIRE LA DIAPOSITIVE —

"IL EST ESSENTIEL DE BOIRE ET DE MANGER"

11

Dans le cadre de tout traitement, il est essentiel de faire manger l'enfant qui a la rougeole et de montrer à la personne qui s'en occupe certaines préparations spéciales. Dans plusieurs des études cliniques réalisées sur les complications de la rougeole, on a relevé un facteur fondamental : les pertes pondérales des jeunes enfants et la fréquence avec laquelle des signes de malnutrition protéino-calorique apparaissaient chez les survivants de la rougeole. La moindre résistance à la diarrhée, la pneumonie et les autres maladies suivant la rougeole peuvent se maintenir pendant un an et peuvent être partiellement attribuables à la malnutrition protéino-calorique de laquelle ces enfants risquent de ne jamais se récupérer, à moins que des mesures particulières soient prises pour accroître de façon active le gain pondéral dès les épisodes initiaux de la rougeole. Les mères et les autres membres de la famille ne doivent pas s'arrêter de donner à manger aux enfants souffrant de rougeole. Dans la mesure du possible, la quantité et la fréquence des repas doivent être accrues en utilisant des aliments riches en calories et en nutriments. Le gain pondéral de l'enfant doit être suivi avec fréquence. Afin de motiver les personnes s'occupant des enfants pour qu'elles continuent de les soigner, il faut leur préciser que le risque de mortalité ne disparaît pas aussi vite que les éruptions ou la fièvre.

"CONSEILS DE NUTRITION"

12

Expliquer à la mère, ou en général à la personne qui s'occupe de l'enfant, que la rougeole affaiblit considérablement l'enfant. Lui rappeler de lui donner à manger plus et plus souvent. Si l'enfant souffre de diarrhée, lui donner plus de liquides. Les aliments spéciaux ou les compléments coûteux ne sont généralement pas nécessaires pour les enfants qui se récupèrent de la rougeole. Les aliments traditionnels préparés avec des préparations de sevrage fort répandues localement peuvent être fortifiés avec des ingrédients riches en énergie, protéines, vitamines et minéraux. Il faut montrer aux personnes qui s'occupent des jeunes enfants quels types et quelles quantités d'aliments leur donner. Les enfants doivent être pesés chaque semaine ou chaque mois.

"COMPLICATIONS"

L'enfant qui souffre de rougeole doit être examiné et surveillé pour prévenir toute complication. Pour sauver sa vie, il est nécessaire de traiter la maladie sans attendre. L'OMS a publié des lignes directrices pour le traitement de certaines complications de la rougeole, dont la diarrhée et les infections respiratoires. Passons brièvement en revue certains des points importants.

— LIRE LA DIAPOSITIVE —

"PNEUMONIE, STRIDEUR\CROUP"

— LIRE LA DIAPOSITIVE —

"LESIONS OCULAIRES"

— LIRE LA DIAPOSITIVE —

"DIARRHEE/DESHYDRATATION"

— LIRE LA DIAPOSITIVE —

"PRODUITS NECESSAIRES"

— LIRE LA DIAPOSITIVE —

"VACCINATION"

18

Nous commençons à affecter de nouvelles ressources à l'amélioration du traitement de la rougeole, mais il ne faut pas oublier qu'il vaut mieux prévenir que guérir. En fait, la vaccination universelle est la principale intervention pour une lutte efficace et durable contre la rougeole. L'élément de plus déterminant face au risque de mortalité et de morbidité est l'état de vaccination. La vaccination universelle est la solution permanente contre la rougeole. En dépit de cela, la couverture est nettement inférieure à 100 %.

"AUGMENTATION DE LA COUVERTURE VACCINALE"

19

Des efforts plus intenses sont nécessaires pour accroître la couverture. Voici une synthèse des principes de base.

— LIRE LA DIAPOSITIVE —

"OBJECTIFS POUR 1995"

20

Durant les deux dernières années, la rougeole a tué plus de 3 millions d'enfants. Outre ces décès, les enfants qui ont survécu l'infection initiale ont subi une incidence de la maladie et de la mortalité dix fois supérieure à celle des enfants n'ayant pas souffert de la rougeole. C'est pourquoi l'UNICEF considère la rougeole comme "l'une des menaces les plus mortelles contre les enfants durant les années 90". De récents travaux de recherche révèlent qu'il existe un espoir pour les enfants qui contractent la rougeole : l'administration de vitamine A et le traitement rapide des complications doivent devenir des pratiques universelles. Il est également essentiel de former les mères pour qu'elles puissent contribuer à la récupération nutritionnelle de l'enfant ayant souffert de la rougeole, compte tenu du degré élevé de morbidité et de mortalité qui persiste, dans certains cas même un an après l'infection. La stratégie décrite dans ce diaporama peut fortement contribuer à réaliser les objectifs fixés pour 1995 au Sommet mondial pour les enfants de 1990.

— LIRE CITATIONS SUR LA DIAPOSITIVE —

En résumé, toute stratégie complète de lutte contre la rougeole doit comprendre un traitement efficace et une prévention sous forme de vaccination.

— LIRE STRATEGIE SUR LA DIAPOSITIVE —

" EL MANEJO DEL SARAMPION Y LA VITAMINA A"

Muchos infantes y niños mueren anualmente de complicaciones asociadas con el sarampión. En una comunidad asiática, cada muerte asociada con el sarampión se conmemora con una estatuilla de madera como ofrenda a la diosa del sarampión conocida como "mata".

— SEÑALE HACIA LA DIAPOSITIVA —

Hoy en día, las muertes causadas por el sarampión se pueden prevenir. El propósito de esta presentación es actualizar a los profesionales y para-profesionales de salud en el manejo de los casos de sarampión, incluyendo una nueva manera de reducir las complicaciones y la mortalidad relacionadas con el sarampión mediante la administración de dosis altas de vitamina A. Las diapositivas se pueden utilizar como parte de un curso formal o como parte de una sesión informal de introducción o actualización para profesionales o para-profesionales. La presentación contiene una revisión de los elementos esenciales del manejo de casos. Enfatiza aspectos nuevos tales como la complementación con vitamina A, incluyendo los resultados de estudios en los cuales se identificó la asociación de la vitamina A con el sarampión y se comprobó el efecto del tratamiento con vitamina A. También ofrece una guía práctica sobre temas como el diagnóstico de las complicaciones, los materiales necesarios en los servicios de salud, las dosis para diferentes grupos de edad, y las preparaciones de vitamina A y cómo administrarlas.

"CAUSAS DE MORTALIDAD INFANTIL"

A pesar de la disponibilidad de una vacuna muy efectiva, el sarampión aún es responsable de más muertes que la combinación de todas las demás enfermedades prevenibles por inmunización que están cubiertas por el Programa Ampliado de Inmunizaciones (PAI). En los países en vía de desarrollo, la letalidad por sarampión es 20 veces más alta que en los países desarrollados. Estudios de epidemias en comunidades entre 1961 y 1990 muestran tasas de letalidad entre 1,5 y 30 por ciento. Se creía que las tasas de mortalidad altas asociadas con el sarampión ocurrían solamente en Africa, pero recientemente se han informado tasas altas en Latinoamérica y Asia. Algunos de los factores importantes que contribuyen a la alta mortalidad en los países en vía de desarrollo incluyen: edad temprana en el momento de la infección, pobreza, hacinamiento e intensidad de la exposición, y atención médica tardía o ausente. Recientemente se ha identificado el estado nutricional, especialmente el estado de vitamina A, como un factor crítico.

"CONSECUENCIAS DEL SARAMPION"

Las muertes relacionadas con el sarampión ocurren principalmente a causa de complicaciones como la neumonía, la diarrea y el crup. Otras complicaciones del sarampión, especialmente la ceguera, la otitis media, la encefalitis y el retraso en el crecimiento, producen incapacidad de por vida. La incidencia de morbilidad y mortalidad (por otras enfermedades de la niñez) en los meses que le siguen a una epidemia de sarampión puede llegar a ser diez veces más alta en los sobrevivientes al sarampión. Así, el sarampión no solamente puede causar la muerte y complicaciones durante su fase aguda, sino que los efectos a largo plazo después de la enfermedad se pueden ver en la reducción de los índices de sobrevivencia de los niños durante un período de varios meses. Los que sobreviven la enfermedad aguda tienen una probabilidad más alta de morir por varias causas, cuando se comparan con los que no tuvieron el sarampión. Entre menor es la edad del niño en el momento de la infección mayor es la mortalidad a largo plazo.

"IMPACTO DE LA VITAMINA A"

La mitad de los casos de ceguera en Africa se pueden atribuir al sarampión. Estudios en Africa y Asia muestran que los niveles bajos de vitamina A en la sangre incrementan el riesgo de muerte en los niños. Se ha informado sobre niveles bajos de retinol en la sangre de pacientes con sarampión, no solamente en lugares en donde la deficiencia de vitamina A es un problema serio, sino también en áreas en donde no se observan comúnmente signos clínicos de dicha deficiencia. Recientemente, tres estudios clínicos con utilización aleatoria de complementos de vitamina A han demostrado en forma concluyente que el tratamiento de los casos severos de sarampión con por lo menos dos dosis de 200.000 UI de vitamina A por vía oral reduce la severidad y la duración de las complicaciones y disminuye la mortalidad.

— SEÑALE LA GRAFICA —

La Organización Mundial de la Salud (OMS) ha divulgado recomendaciones para administrar rutinariamente vitamina A por vía oral a los niños con sarampión severo.

"EL SARAMPION Y LA VITAMINA A"

— LEA LA DIAPOSITIVA —

"MANEJO DE LOS CASOS"

— LEA LA DIAPOSITIVA —

"ES SARAMPION?"

El primer paso en el manejo del sarampión es la oportuna y adecuada identificación de todos los casos. El sarampión se puede diagnosticar como se muestra aquí.

— LEA LA DIAPOSITIVA —

En resumen, la definición del caso clínico para el diagnóstico del sarampión es: fiebre de mas de tres días con un brote característico, y por lo menos uno de los siguientes síntomas: tos, secreción nasal, ojos rojos.

"PLAN DE TRATAMIENTO CON VITAMIMA A"

Aquí se muestra el protocolo de tratamiento con vitamina A para el sarampión. De acuerdo con algunos estudios que se han publicado, la dosis que se recomienda aquí se absorbe suficientemente para tener impacto, a pesar de que el sarampión se acompaña frecuentemente de diarrea. Los niños menores de 12 meses y los que pesan menos de 8 kilos reciben la mitad de la dosis, o sea 100.000 UI en lugar de 200.000 UI.

"ADMINISTRACION DE LA VITAMINA A"

La vitamina A se encuentra en cápsulas o en un líquido concentrado. Los niños mayores pueden ingerir una cápsula que contiene 200.000 UI. A los niños menores de dos años se les debe escurrir el contenido de la cápsula directamente en la boca. El número de gotas en una cápsula de vitamina A varía de 6 a 8. Cuando se destapa un nuevo lote de cápsulas, se debe medir el número de gotas cortando una cápsula y contando el número de gotas que contiene. El contenido total de una cápsula es igual a una dosis de 200.000 UI. Para niños menores de 12 meses, se abre la cápsula y se exprime la mitad del número de gotas directamente en la boca. Esto es equivalente a una dosis de 100.000 UI. Este método también se puede utilizar en aquellos niños que están demasiado enfermos para ingerir la cápsula.

"COMPLEMENTOS DE VITAMINA A"

La complementación con vitamina A de los casos de sarampión se puede adaptar fácilmente a los programas de atención primaria de salud porque tiene las siguientes ventajas: se puede administrar fácilmente por vía oral y no se necesitan inyecciones; el complemento no necesita refrigerarse; y tiene un tiempo de vida bastante largo — 2 años en un frasco sin destapar y 6 meses después de destaparlo.

— LEA LA DIAPOSITIVA —

"LA ALIMENTACION Y LA ADMINISTRACION DE LIQUIDOS SON CLAVES"

La alimentación del niño con sarampión y la enseñanza de la persona que cuida el niño en la casa acerca de la alimentación especial son elementos críticos para todos los pacientes. Un factor clave que se observó durante los estudios clínicos sobre las complicaciones del sarampión fue el grado de pérdida de peso y la frecuencia de signos clínicos de desnutrición proteínico-calórica en los sobrevivientes. La menor resistencia a la diarrea, la neumonía y otras enfermedades después de un episodio de sarampión puede continuar hasta por un año y se puede atribuir, por lo menos en parte, a la desnutrición proteínico-calórica de la cual a veces no se recuperan los niños si no se toman medidas especiales para incrementar activamente la ganancia de peso después del episodio de sarampión. Las madres u otros familiares no deben dejar de alimentar al niño con sarampión. Si es posible, la cantidad y la frecuencia de las comidas se debe incrementar utilizando alimentos ricas en calorías y de alto nivel nutricional. El peso del niño se debe vigilar frecuentemente. Para motivar a la persona que cuida del niño a proveer atención continua en el hogar al niño sobreviviente de sarampión, se le debe enfatizar que el riesgo de muerte no desaparece con la desaparición del brote y la fiebre.

"MENSAJES NUTRICIONALES"

— LEA LA DIAPOSITIVA —

Explíquele a la madre o persona que cuida al niño que el sarampión deja muy débil al niño. Recuérdele que debe alimentarlo más y con mayor frecuencia. Si hay diarrea, hay que darle más comida y más líquidos. Las comidas especiales o los complementos costosos por lo general no son necesarios para el niño que se está recuperando del sarampión. Los alimentos tradicionales, es preparaciones comunes del destete, se pueden enriquecer agregándoles ingredientes ricos en calorías, proteínas, vitaminas y minerales. A las madres o personas que cuidan a los niños más pequeños se les debe enseñar los tipos y cantidades de alimentos recomendables para ellos. Se debe vigilar el peso semanal o mensualmente.

"COMPLICACIONES"

Al niño con sarampión se le debe proteger y mantener bajo observación para detectar complicaciones. El tratamiento a tiempo es clave para prevenir la muerte. La OMS ha formulado recomendaciones para tratar las complicaciones, incluyendo la diarrea y las infecciones respiratorias. Vamos a repasar brevemente algunos de los puntos mas importantes.

— LEA LA DIAPOSITIVA —

"NEUMONIA"

— LEA LA DIAPOSITIVA —

"LESIONES OCULARES"

— LEA LA DIAPOSITIVA —

"DIARREA Y DESHIDRATACION"

— LEA LA DIAPOSITIVA —

"MATERIALES NECESARIOS"

— LEA LA DIAPOSITIVA —

"VACUNACION"

18

A tiempo que se asignan más recursos para mejorar el manejo de los casos de sarampión, no debemos olvidarnos de que la prevención es mejor que la curación. De hecho, la intervención básica para el control efectivo y sostenido del sarampión es la vacunación universal. El más importante determinante de la morbilidad y mortalidad es el estado de vacunación. La vacunación universal es la solución permanente para el sarampión. Sin embargo, con frecuencia la cobertura de vacunación se mantiene muy por debajo del 100 por ciento.

"AMPLIACION DE LA COBERTURA"

19

Se necesitan más esfuerzos para incrementar la cobertura. Este es un resumen de los principios claves:

— LEA LA DIAPOSITIVA —

"METAS PARA 1995"

20

El sarampión ha matado a más de 3 millones de niños en los dos últimos años. Además de estas muertes, los niños que sobreviven la infección inicial sufren de un índice de morbilidad y mortalidad diez veces más alto que el de los que no tuvieron sarampión. Así, UNICEF ha llamado al sarampión "uno de las mayores amenazas de muerte para los niños en la década de los 1990s." Estudios recientes han demostrado que hay esperanza para el niño que ha contraído el sarampión: la administración de vitamina A y el tratamiento oportuno de las complicaciones deben convertirse en prácticas universales. Es también esencial capacitar a las madres en la recuperación nutricional de los niños con historia de sarampión, porque estos niños continúan a alto riesgo de mortalidad y morbilidad hasta un año después de la infección. La estrategia que se ha descrito en esta presentación puede ayudar mucho a alcanzar las metas para 1995 que se formularon en la Cumbre Mundial en Favor de la Infancia efectuada en 1990.

— LEA LA DIAPOSITIVA —

En resumen, una estrategia comprensiva para el control del sarampión debe incluir tanto el manejo efectivo de los casos como la prevención por medio de la vacunación.

— LEA LA ESTRATEGIA DE LA DIAPOSITIVA —

CREDITS \ CREDITS \ CREDITOS

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A Guide for Primary Health Care Programs

MEASLES CASE MANAGEMENT AND VITAMIN A

Introduction

Measles is readily preventable by vaccination. Yet in 1989, 45 million children in developing countries suffered from measles, and of these, 1.4 million died. Deaths from measles occur mainly as a result of complications such as pneumonia, diarrhea and croup (stridor). Other complications of measles, namely, blindness, otitis media, encephalitis and growth failure, result in life-long disabilities. In Africa alone, where the prevalence of blindness in preschool children is estimated at 1 per 1000, measles has been identified as responsible for half of all childhood blindness. The incidence of illness and death (from other childhood illnesses) in the months following an outbreak of measles can be ten times greater in measles survivors. This longer-term impact is only now becoming clear, indicating that the adverse outcomes of measles are more serious than previously imagined.

To date there is no specific cure or treatment for measles itself. Thus, case management guidelines are aimed at the prevention and treatment of its complications: antibiotics for secondary infections, antipyretics for fever, oral rehydration therapy for diarrhea, and eye care for ocular complications. Recent studies in Africa have shown that vitamin A therapy reduces the death rate and complications of severe measles by half. While vitamin A has no direct effect on the measles virus, it prevents or lessens the severity of the complications from measles, presumably through its role as a protector of the immune system and epithelial tissue. Measles lowers the serum vitamin A level, causing a state of vitamin A deficiency, which may not be obvious on clinical examination. It is thought that the functioning of epithelial surfaces of the eye, respiratory and gastrointestinal tracts is damaged when serum vitamin A falls and remains below critical levels, allowing the measles virus and other pathogens to invade these tissues, causing eye damage, diarrhea, pneumonia, croup, and otitis media.

Vitamin A can be effective in reducing deaths and complications from measles when given orally in the form of a concentrated liquid which is dispensed through capsules or a pump-bottle. No special technical skills or equipment are needed. Because the technical and operational requirements for measles treatment with vitamin A are few, it can easily be added to existing measles case management. Each program will need to adapt the vitamin A component to fit into its present policies and practices. Specifically, the following actions should be taken:

- Issue revised or new guidelines on measles case management.
- Train health staff (health workers, supervisors, trainers, managers) on the "why" and "how" of measles case management through short in-service training sessions.
- Procure and distribute supplies, including vitamin A.
- Add information to existing reports and forms to monitor effective measles case management.

It should be emphasized that vitamin A dosing of measles cases should not undermine the importance given to universal immunization, nutritional improvement, or appropriate treatment of the complications of measles. In fact, the primary intervention for effective and sustained measles control is universal immunization. Maintaining adequate nutritional status in young children, especially during the ages of 6 to 24 months, will assure reduced case fatality rates from measles ***and other common diseases of childhood***. Clinical experience to date does suggest, however, that dramatic reductions in measles-related deaths and disabilities can be achieved in the very near term if all children with measles are given oral vitamin A supplements. The costs are minimal.

This packet contains some tools that will facilitate the incorporation of new knowledge about the nutritional management — especially vitamin A supplementation — of measles cases into existing programs. It is assumed that the recipients of this material are familiar with measles immunization guidelines and the case management of measles and its complications. Thus, this packet focuses mainly on newer information about managing measles cases, in particular, the use of vitamin A and emphais on feeding.

The contents of this package are:

- **Measles Case Management**
  (Useful for health care providers at all levels, it summarizes all aspects of measles case management from diagnosis to treatment.)

- **Measles Case Management and Vitamin A: Slides/Handouts and Text**
  (Contains practical information needed by health workers and their supervisors on how to implement the new guidelines for vitamin A supplementation within the context of a comprehensive measles control program.)

- **Vitamin A Supplies: Guidelines**
  (Useful for staff responsible for ordering supplies and maintaining stores.)

- **The Scientific Basis for Using Vitamin A: An Annotated Bibliography**
  (Contains technical information suitable for physicians, researchers, and managers with a technical background.)

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THE SCIENTIFIC BASIS FOR USING VITAMIN A

An Annotated Bibliography

The following studies show that vitamin A lowers measles case fatality. Earlier, this effect was thought to occur only in communities with a high prevalence of clinical vitamin A deficiency (xerophthalmia). However, the results of recent studies, summarized in this bibliography, indicate that the benefits of supplementation for acute or complicated measles cases can be obtained even in areas where clinical vitamin A deficiency is not a problem.

- Barclay A.J., A. Foster, and A. Sommer. 1987. **Vitamin A Supplements and Mortality Related to Measles: A Randomized Clinical Trial. Brit Medical J 294:294-296.** In a clinical trial conducted during the measles season in Tanzania, 180 children under 6 years of age who were admitted to the hospital for measles were randomized to receive either vitamin A treatment (200,000 IU of vitamin A on the day of admission, and another 200,000 IU dose the following day) or the standard management of measles without any vitamin A. Measles mortality in the supplemented group was 6/88 (7%) compared to 12/92 (13%) among the controls. The difference was greatest for children under age 2 years and children with lung disease. The incidence of mortality was several times higher among malnourished children than better nourished children. Vitamin A supplementation reduced mortality in all nutritional groups.

- Coutsoudis, A., M. Broughton, and H.M. Coovadia. 1991. **Vitamin A Supplementation Reduces Measles Morbidity in Young African Children: A Randomized, Placebo-Controlled, Double-Blind Trial. Amer J Clin Nutr 54:890-895.** In Durban, South Africa, 60 infants aged 4 to 24 months (average age 10 to 12 months) with complicated measles were randomly assigned to a vitamin A treatment or placebo group upon admission to the hospital. The children were followed up daily for 8 days in the hospital and thereafter at 6 weeks and 6 months. A dose of 200,000 IU oral vitamin A was given to children over 12 months of age on day 1, day 2, day 8 and 6 weeks after admission; younger children received 100,000 IU instead of 200,000 IU. The results showed a significant reduction in the duration of pneumonia in the supplemented group and complete clinical recovery within 8 days in 96 percent of the treatment group versus 65 percent of the control group.

- Foster, A. and A. Sommer. 1987. **Corneal Ulceration, Measles, and Childhood Blindness in Tanzania. Brit J Ophthalmol 71:331-343.** One hundred and thirty children under the age of 11 years with corneal ulcers were clinically examined to determine the cause of ulceration. Of these children, 40% were under the age of 2 years and 76% were under the age of 5 years. Serum vitamin A measurements showed that 26% of the children had vitamin A deficiency. Measles infection was associated with 29% of corneal ulcers in the under 2 year olds, 70% in the 2 to 4 year olds, and 37% in the 5 to 10 year olds.

- **Hussey, G.D. and M. Klein. 1990. A Randomized Controlled Trial of Vitamin A in Children with Severe Measles. The New England J Medicine 323:160-164.** A randomized, double-blind, placebo-controlled vitamin A intervention trial was conducted on 189 non-xerophthalmic children with acute measles in Cape Town, South Africa. Two doses of 200,000 IU each were administered to the treatment group with a one-day interval between doses. Of the 12 children who died, 10 were among those given the placebo. Treated children recovered more quickly from pneumonia and diarrhea, had less croup, and spent fewer days in the hospital. These results were statistically significant.

- **Markowitz, L.E., N. Nzilambi, W.J. Driskell et al. 1989. Vitamin A Levels and Mortality Among Hospitalized Measles Patients, Kinshasa, Zaire. J Trop Pediatrics 35:109-112.** Serum vitamin A levels were studied in 283 children hospitalized for measles between the ages of 4 and 60 months (median 12) in Kinshasa, Zaire. Seventy-one children died during hospitalization. Children below 24 months of age with vitamin A levels under 5 ug per dl had a significantly greater risk of dying than those with higher levels.

- **Reddy V., P. Bhaskaram, N. Raghuramulu et al. 1986. Relationship Between Measles, Malnutrition, and Blindness: A Prospective Study in Indian Children. Amer J Clin Nutr 44:924-930.** In a prospective study of 1,544 slum children under the age of 5 years carried out in Hyderabad, India, weight and height measurements were taken at baseline, and morbidity data were collected weekly over a 15-month period. In all, 318 cases of measles were identified, of which 281 were followed for 6 months after recovery. Corneal lesions were observed in 3% of the measles cases. Serum vitamin A levels were seriously depressed in the children with measles. Nearly 60% of the children developed bronchopneumonia or diarrhea during the acute stage of measles, and over three times as many children with measles developed severe malnutrition, as age- and weight-matched controls without measles.

Discussion

Recent research has shown that in addition to preventing blindness, vitamin A is an important factor in preventing infant and child mortality. The lining membranes of the body (especially epithelial surfaces) and the immune system need vitamin A in order to function normally and remain healthy. Blood levels of vitamin A are low in all children with measles. The reason for this is not known. The body stores vitamin A in the liver and it seems that measles interferes with the release of these stores into the blood. When vitamin A levels are low, these tissues are no longer able to protect the body effectively from attack by microbes in the environment. The ability of tissues to repair themselves after such an attack is also reduced. The result is an increased severity of infections, more serious complications, and increased risk of death.

These studies show that vitamin A lowers measles case fatality rates not only in communities where signs of vitamin A deficiency are commonly seen but also in areas where the deficiency may be marginal or sub-clinical. These studies also pointed out the following:

- Diarrhea did not appear to reduce the effectiveness of the oral supplements sufficiently to impair impact. Measles patients with complications of diarrhea should receive the same dose of vitamin A as other measles patients.

- The greatest benefit from vitamin A supplementation may occur in children under 2 years of age. However, the benefits of supplementation were shown in children up to the age of 6 years. Therefore, all complicated or acute measles cases should be supplemented with vitamin A.

- Measles is closely linked to malnutrition, which predisposes to death from measles and also results from measles. Persuading mothers to actively increase the food intake of children who are recuperating from measles can save additional lives. Therefore aggressively treating measles with nutritional therapies — including vitamin A supplementation during acute measles and extra feeding during recuperation — has strong justification.

- Measles and vitamin A deficiency are important factors in childhood blindness. In measles patients, the risk of corneal ulceration may remain high for several weeks after measles infection. This is associated with vitamin A deficiency, herpes simplex infection, measles virus invasion of the eyes, and the use of harmful, traditional eye medications.

VITAMIN A SUPPLIES
Guidelines

It is critical to maintain an assured, uninterrupted supply of vitamin A supplements up to the point of distribution. Many programs have suffered from disruptions in vitamin A supplement distribution because of insufficient planning and underestimations of the time lags between reorder and receipt of the supplies needed to replenish distribution sites.

Types of Preparations

Two forms of vitamin A preparations are suitable for measles treatment:

- **Gelatin capsules containing a liquid concentrate of vitamin A.** The most commonly used preparation is the 200,000 IU capsule, which also has 40 IU of vitamin E for improved stability and absorption. For smaller children who cannot swallow the capsule, the health worker snips off the end of the capsule and squeezes out its contents directly into the child's mouth. The number of drops in a capsule of vitamin A may vary from 6 to 8. When each new batch of capsules is unpacked, the health worker should count the number of drops by cutting open a capsule and squeezing out the contents. The full contents of each capsule equal one dose of 200,000 IU. To reduce the dose to 100,000 IU (for 6 to 11 month old infants), half the number of drops are squeezed out and discarded first, and the remaining amount is given to the child. 200,000 IU capsules are generally available in bottles of 500 and 100 capsules each, and the cost per capsule is approximately 2 U.S. cents. Bottles containing 100 capsules may be especially useful for peripheral health units because of the loss of potency that can occur once the bottle has been opened.
- **A dispenser bottle with pump containing a liquid or syrup.** This alternative to the capsule, which is being developed by WHO and UNICEF, delivers a pre-calibrated amount of the liquid concentrate directly into the mouth of the child. The chief advantages are that the dispenser delivers a more accurate dose of 100,000 IU, and is quicker and less messy. It is also likely to be cheaper.

Over-the-counter preparations such as multivitamin supplements distributed through health services or through retail sales in most countries are inadequate for the treatment of measles.

Sources

UNICEF is the principal supplier of vitamin A supplements. In addition to the 200,000 IU capsule, UNICEF can provide capsules of other strengths (e.g.,100,000 IU or 50,000 IU).

UNICEF often provides vitamin A supplements as part of its agreed program of cooperation with a country's health program, sometimes as a component of kits of essential drugs. If such an arrangement does not exist already and cannot be agreed upon, UNICEF can, for a small fee, provide vitamin A supplements to governments or agencies. A normal delivery time of 6 to 9 months should be allowed, but in an emergency, supplies can be provided in a few days. Agencies interested in obtaining vitamin A supplies should contact the local UNICEF office located in the capital city of the country.

Additional amounts of vitamin A for experimental purposes and emergency relief have also been provided free of charge by Task Force Sight and Life, Basle, Switzerland, a non-profit agency funded by Hoffman-LaRoche.

Estimating Requirements

A critical element for the success of vitamin A supplementation is to obtain an assured supply of supplements and have them ready for administration by staff who make first contact with measles cases - in the home, community, health post, clinic or hospital. By following the steps shown here, a one-year supply can be estimated. Although the expected number of cases is estimated in relation to the size of the birth cohort, not all cases will occur in the first year of life.

Step 1:

Estimate the number of measles cases to be managed by the health facility, or in the program area, over a 12-month period. If this information is not available from hospital or clinic records, follow step 2. If this information is available, go to step 3.

Step 2:

If no other basis exists for estimating the number of measles cases, assume that children in the birth cohort (0 to 11 months old) comprise 4% of the total population. In the absence of measles immunization in the area, the expected number of measles cases is all these children. To determine the number of expected measles cases in one year, estimate the proportion of infants protected by immunization, which is the coverage multiplied by a vaccine efficacy of 85%. This is subtracted from the 4% of the total population. If measles immunization 2coverage data are not available, assume 60% coverage. Round off the final number of expected measles cases to the nearest ten.

Step 3:

Multiply the number of cases by 2 for the number of doses to be given.

Step 4:

Add allowances for unanticipated need (for example, measles epidemic or for treatment of xerophthalmia cases), wastage, need for end-of-year reserve, and because capsules come in 100- or 500-dose bottles.

Step 5:

Estimate how many 100-capsule or 500-capsule bottles will be needed. (*See box below*)

NOTE: A re-order level should be estimated for local inventories and every effort made to fill requisitions for vitamin A supplies in a timely manner. Vitamin A distribution often suffers from intermittent and inadequate supplies.

EXAMPLE:
Estimating Requirements

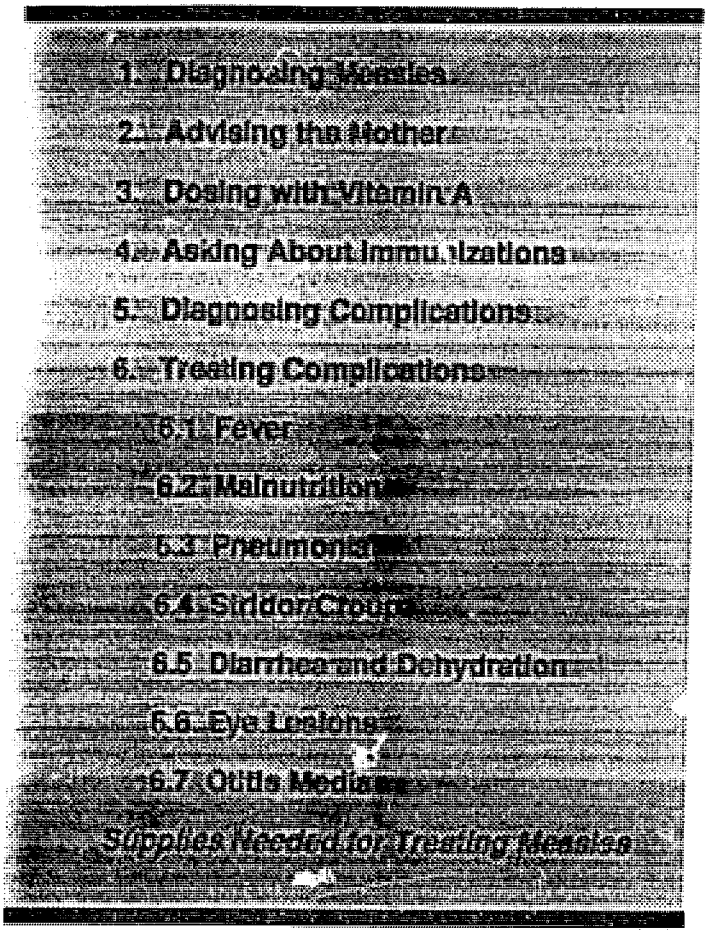
Step 1. Total population of the area served	=	10,000
Step 2. Birth cohort of 4%	=	400
–Percent of infants protected is immunization coverage of 60% x 85% efficacy, which equals 51% of infants	=	204
–Expected number of cases is the birth cohort minus protected children, 400-204	=	196
–Round off to	=	200
Step 3. Number of capsules at 2 doses/case	=	400
Step 4. Number of capsules needed per year (includes 50% extra allowance for wastage, etc.)	= 400 x 1.5 =	600

Step 5. Requirement is 2 bottles of 500 capsules each,or 6 bottles of 100 capsules each.

Storage and Care of Supplies

Vitamin A capsules are usually packaged in opaque glass bottles to reduce the effect of light and temperature. Because vitamin A must be protected from sunlight, do not transfer capsules to ordinary transparent containers. Vitamin A preparations are more stable than vaccines and do not require refrigeration. Vitamin A should not be frozen. Distribution to field sites can be made as infrequently as once a year. The shelf life of capsules in an unopened bottle is two years. Each container should have an expiration date. Once the bottle is opened there is gradual degradation, and supplies in opened containers should be used up within 6 months, if possible. Because vitamin A has a finite shelf life, containers should be dated and labelled, and a "first in, first out" method of dispensing should be used. New stocks should be placed behind old stocks to facilitate rotation.

MEASLES CASE MANAGEMENT



The information contained in this section is based on material in the following documents:

The Treatment and Management of Severe Protein-energy Malnutrition, World Health Organization, Geneva, 1981.
Acute Respiratory Infections in Children: Case Management in Small Hospitals in Developing Countries: A Manual for Doctors and Senior Health Workers. World Health Organization, Geneva, 1990.
A Manual for the Treatment of Diarrhea: For Use by Physicians and Senior Health Workers. World Health Organization, Geneva 1990.

1. Diagnosing Measles

There is no rapid laboratory diagnosis test for measles. A simple clinical case definition for diagnosis of measles is:

> **Fever for more than three days with a characteristic maculo-papular rash, and at least one of the following — cough, runny nose, red eyes.**

Diagnosing the complications of measles involves two steps: taking a history and clinical examination, as described below:

Taking a History

— Ask about:

1. Breastfeeding, and whether the child is taking weaning foods?
2. Is the child able to drink?
3. Cough, fast breathing or chest indrawing — symptoms of pneumonia.
4. Diarrhea — defined as three or more loose stools a day
5. Discharge from eyes or ears — symptoms of conjunctivitis and otitis media.
6. Abnormal sleepiness — may be due to dehydration or encephalitis, or it may be a symptom of a severely ill child.

Clinical Examination

— Check especially:

1. Temperature.
2. Weight — If possible enter weight on a growth chart. Where previous weight measurements are available, weight loss can be an indicator both of dehydration and malnutrition.
3. Signs of dehydration—dry mucous membranes, loss of skin elasticity, restlessness.
4. Breathing rate and chest indrawing —Fast breathing with chest indrawing are signs of severe pneumonia.
5. Eyes for corneal damage —the normally clear and black central part of the eye may become opaque or be damaged.
6. Ears for discharge—may only be visible by examination.
7. Mouth — for ulcers.

2. Advising the Mother

The child will be weak and prone to infections for some time. In uncomplicated measles, fever will fall within a week and the rash will fade in 10-14 days. But increased risk of illness and death may last for at least a year after measles. Mothers should be encouraged to seek help for treatment of illness as early as possible during this period.

- **Continue breastfeeding**, or try to give as much as the child can take of weaning foods and fluids at frequent intervals. Feeding high energy foods which are not too bulky, as well as yellow fruits and vegetables and dark green leaves, is important during recovery from measles.

- **Control fever** to reduce the risk of convulsions, by keeping the child at as normal a temperature as possible.

- **Bring the child back** for further treatment if:

  1. General condition worsens.
  2. Breathing becomes rapid or difficult.
  3. Diarrhea continues or signs of dehydration appear.
  4. Child is not able to drink.
  5. Eyes become painful, cloudy or there is change in vision.

3. Dosing with Vitamin A

Giving vitamin A saves lives in the acute stage of measles. Vitamin A also reduces the severity of many complications of measles in the long term. Give vitamin A supplements to all children with measles:

- In areas where measles case fatality is known to be high.[1]

- In areas of known vitamin A deficiency.[1]

---

1 (ED.NOTE: All rural and low-income urban communities in developing countries are at high risk of falling into these categories. Conducting studies to determine measles case fatality rates and vitamin A deficiency prevalence involve expensive and technically complex studies. Managers of primary health care programs will need to make their own decisions regarding the appropriateness of investing resources in such studies if current data do not exist, or whether to begin dosing all measles cases with 2 doses of vitamin A on the assumption that the conditions noted above are likely to prevail in their communities.)

- In any case of severe or complicated measles. Vitamin A supplements should be used for children with severe measles even in industrialized countries such as the U.S. or countries in Europe.

Vitamin A supplements are available either as capsules (50,000 IU, 100,000 IU or 200,000 IU) or in liquid form with a pump dispenser. Check the instructions on the labels before use. Capsules need to be opened for children under the age of two years. Capsules have the advantage that they can be given to mothers for use at home.

- Give the first dose of vitamin A directly to the child.

VITAMIN A FOR MEASLES SCHEDULE

	Immediately on diagnosis	Following day
Infants under 12 months	100,000 IU	100,000 IU
Children one year and older	200,000 IU	200,000 IU

- Have the mother watch you carefully if she will be required to give the next dose at home. Make sure she understands the need for a dose on the following day.

4. Asking about Immunizations

Ask about the immunization status of the child with measles and other children in the family. Each contact is an opportunity to update immunizations and to give booster doses.

5. Diagnosing Complications

A child with severe or complicated measles will need special treatment. In some situations, such children will need referral. A child has severe or complicated measles, if on examination, it has any of the signs listed in the box below:

SIGNS	DIAGNOSIS
Recent severe weight loss	Dehydration and/or malnutrition
Cough with rapid breathing or Chest indrawing	Pneumonia
Three/more loose stools a day	Diarrhoea
Damaged or opaque central, black part of eye	Potentially blinding eye lesion
Discharge from ears	Otitis media
Convulsions, coma	Encephalitis

6. Treating Complications

Many complications are associated with severe measles, however, these guidelines are for management and treatment of the most common ones. These include malnutrition, pneumonia, diarrhea, eye lesions, and otitis media. A child with complications of measles can be treated successfully. If seen early enough, almost all children can recover.

6.1 Fever

1. Giving paracetamol is the most effective way to reduce fever. Give paracetamol when the child feels very hot or the temperature under the arm is 39°C. Paracetamol has fewer side effects than aspirin.

2. When a child has a convulsion due to high fever, the temperature can be brought down rapidly by sponging the child with a cloth soaked in cold water. In addition, give paracetamol every 4-6 hours.

NOTE: Fever alone is not an indication for treatment with antibiotics.

6.2 Malnutrition

Children with measles become malnourished because:

- Appetite is poor due to fever and general illness.
- Feeding may be difficult due to mouth sores.
- Absorption of food is reduced due to diarrhea.
- There is increased demand for all nutrients both in the acute and recovery phases.
- There is a mistaken custom to stop feeding or reduce feeding in children with measles.

Children with complications following measles need both sufficient fluids and a high quality diet. Dealing with malnutrition will depend on its degree as well as the age of the child. The following are general guidelines to follow for severely malnourished children:

1. Encourage mothers to continue breast feeding.
2. Feed frequently, at least every two hours if possible.
3. For severely malnourished infants and children, start with 125 ml/kg of body weight of half-strength milk feeds. As the child's appetite increases, raise the amounts to 150 ml/kg of body weight of full-strength milk feed.
4. Add vegetable oil and sugar to milk feeds or weaning mixes in order to increase the energy content.

If admitted to hospital, weigh the child daily to follow progress. Weight gain in the intensive phase of rehydration can be marked. After rehydration, "catch-up" growth should still be very rapid with children given high energy feeding regimes. Feeding through a naso-gastric tube may be life saving for children with very severe malnutrition.

FOR FURTHER DETAILS SEE: *The Treatment and Management of Severe Protein-Energy Malnutrition*, World Health Organization, Geneva, 1981.

6.3 Pneumonia

Diagnosis:

- **Pneumonia** signs are cough and fast breathing. The child must be calm while you are looking and listening to its breathing.
- **Severe pneumonia** signs are cough, fast breathing and chest indrawing. Fast breathing is: 50 breaths per minute or more in a child aged 2 months up to 12 months, 40 breaths per minute or more in a child aged 12 months up to 5 years. Chest indrawing is: a definite inward motion of the lower chest wall, seen between the ribs on breathing in.
- When **pneumonia is very severe**, children may be unable to drink. There may also be blueness of the lips and mouth (central cyanosis) due to insufficient oxygen in the blood.

Treatment:

1. Treat pneumonia at home with an oral antibiotic such as cotrimoxazole, amoxycillin, or ampicillin.
2. Advise the mother to return if the condition worsens, and breathing becomes more rapid or difficult.
3. If pneumonia is very severe then admit, if possible, to hospital for intramuscular or intravenous antibiotics.
4. Children with severe pneumonia should be given oxygen if available.
5. Wheezing due to pneumonia will also be helped by antibiotics. Do not use a bronchodilator such as salbutamol. Do not use steriods for treating wheezing due to pneumonia.

6.4 Stridor or Croup

Diagnosis:

- Stridor is a harsh noise on breathing in. It is caused by inflammation of the larynx, trachea or epiglottis.
- Croup is characterized by stridor in a calm child, chest indrawing and hoarseness. The danger of croup is that severe obstruction to breathing may occur.

Treatment:

1. Treat severe croup with an antibiotic. Use chloramphenicol, if available.
2. Severe croup is a medical emergency. Always give an antibiotic immediately, even if a child is to be referred to a hospital.

FOR FURTHER DETAILS SEE: *Acute Respiratory Infections in Children: Case Management in Small Hospitals in Developing Countries. A Manual for Doctors and Senior Health Workers.* World Health Organization, Geneva, 1990.

6.5 Diarrhea and Dehydration

The three rules for treating diarrhea at home are:

1. Give the child more fluids than usual to prevent dehydration.
2. Give the child plenty of food to prevent undernutrition. Encourage the mother to continue breast feeding.
3. Take the child to the health worker if the child does not get better in three days, or develops any of the following:

   —Increase in number

   —Repeated vomiting of watery stools

   —Marked thirst

   —Blood in the stool

If the child will be given oral rehydration solution (ORS) at home:

- Show the mother how much ORS to give after each loose stool and give her enough packets for two days.
- Show the mother how to mix and give ORS.
- Give a teaspoon of ORS every 1-2 minutes for a child under 2 years, frequent sips from a cup for an older child.
- If the child vomits, wait 10 minutes and then continue giving ORS, but more slowly.

To treat severe dehydration quickly:

- **If you have been trained to give intravenous fluids,** start them immediately. If the child can drink, give ORS by mouth while the drip is being set up. Re-assess every 1-2 hours. If there is no improvement, give the intravenous drip more rapidly.

- **If you cannot give intravenous fluids**, then rehydrate with ORS solution (20 ml/kg of body weight) using a naso-gastric tube.
- **If neither intravenous fluids nor naso-gastric tube are possible**, refer immediately.

If blood is present in stool:

Treat for five days with an oral antibiotic recommended for shigella in your area.

FOR FURTHER DETAILS SEE: *A Manual for the Treatment of Diarrhea: For Use by Physicians and Senior Health Workers.* World Health Organization, Geneva 1990.

6.6 Eye lesions

For conjunctivitis (red or sticky eyes):

Teach the mother to:

1. Clean the eyes with cotton or clean piece of cloth.
2. Use tetracycline eye ointment, three times a day for seven days. The mother should:
   - Wash the hands before and after applying eye ointment
   - Pull the lower lid down so that the conjunctiva can be seen
   - Put a little amount of the medicine at the outer third of the lower conjunctiva
   - Keep the eye closed for at least two minutes
3. Avoid applying other remedies.

For corneal damage:

1. Immediately give oral vitamin A supplements - two doses with a 24-hour interval between them, as for treatment of all measles and a third dose after four weeks.
2. Use tetracycline eye ointment 1%, three times a day for seven days.
3. Apply a protective eye pad.

If there is no improvement within three days, refer if possible to a specialist eye worker.
NEVER USE EYE OINTMENTS CONTAINING STEROIDS FOR MEASLES PATIENTS.

6.7 Otitis Media

1. Clean out the discharge from the ears only with cotton or a clean piece of cloth. Do not use instruments to clean out the ears, to avoid the risk of perforation.

2. Give an oral antibiotic such as amoxycillin or ampicillin.
3. Advise the mother to avoid applying oil or other remedies, and use of objects to remove the discharge.

Some Basic Supplies Needed for Treating Complications of Measles

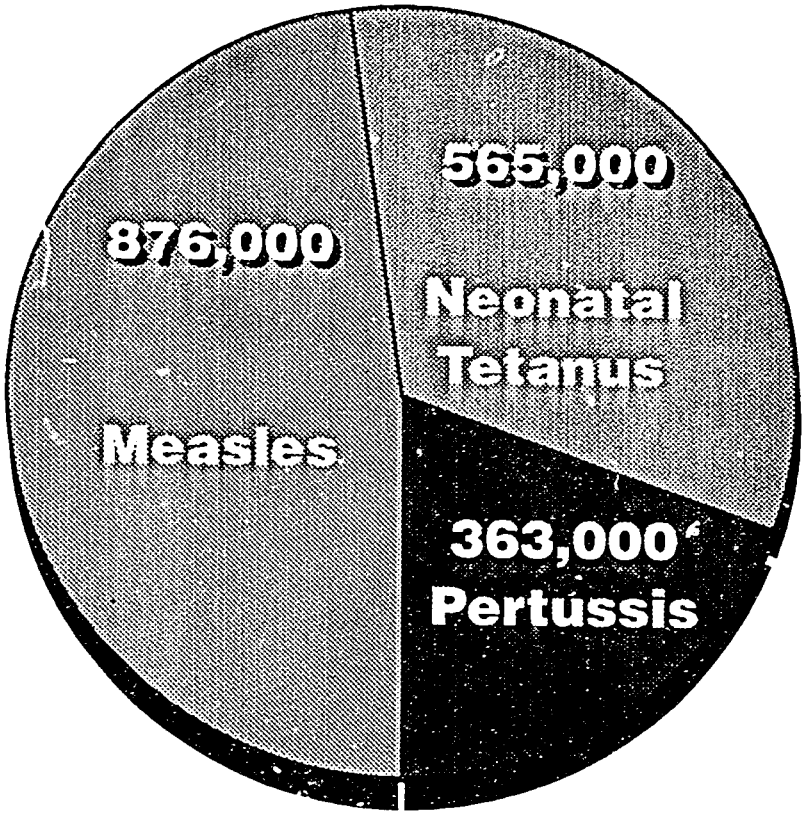
Paracetamol	Tab 100 mg
Vitamin A	Caps 200,000 IU ,100,000 IU
Cotrimoxazol	Tab 80 mg
Amoxycillin	Caps 250 mg
ORS (oral rehydration salts)	Sachet for 1 litre
Tetracycline	Eye ointment 1% tube (5g)

vital slide presentation

Measles Case Management

2

Causes of Child Mortality



Estimated deaths from EPI target diseases (1991)

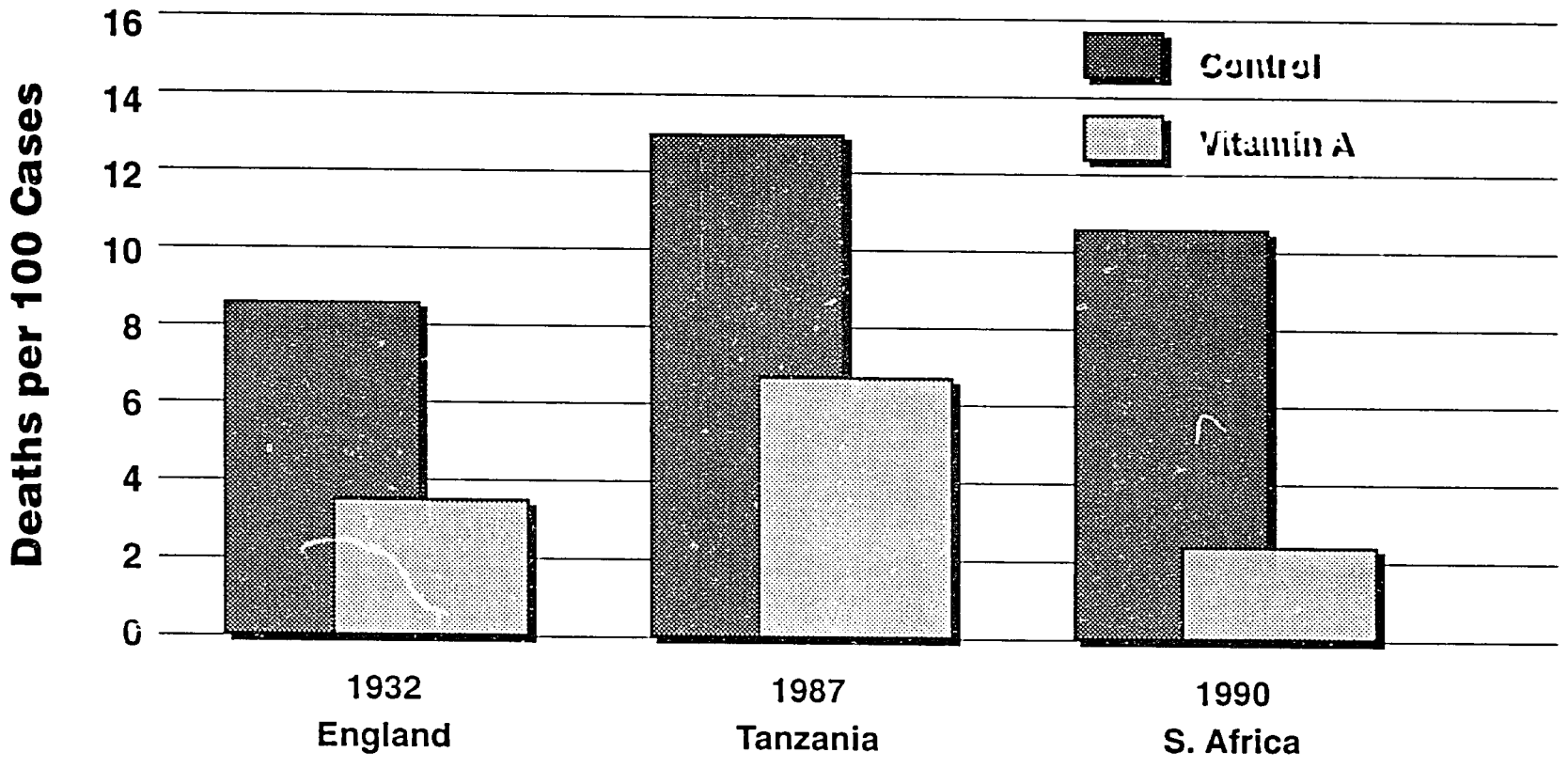
VITAL

Measles Outcomes

- **Deaths** ← pneumonia, diarrhea, croup, other infections
- **Disabilities** ← blindness, otitis media, encephalitis
- **Growth Failure** ← malnutrition

Impact of Vitamin A

- Measles → Blindness
- Measles..... ↓ Serum retinol



VITAL

Measles and Vitamin A

In measles patients.....

- Serum vitamin A ↓
- Immune reactions ↓
- Epithelium weakened, pathogens invade
- Severe diarrhea, ARI, corneal damage

Oral vitamin A raises serum retinol levels and limits eye damage, complications, and deaths.

Case Management

- Diagnosing measles
- Dosing with vitamin A
- Advising the mother
- Asking about immunizations
- Diagnosing complications
- Treating complications

Is It Measles?

DAYS 1-3

The child has a cold, a cough and some fever. The eyes are pink and watery and sensitive to light.

A rash appears across the forehead.

A rash appears behind the ears.

DAYS 3-4

The eyes are pink and covered with sticky yellow fluid.

The rash covers the face.

The rash spreads all over the body

DAYS 4-6

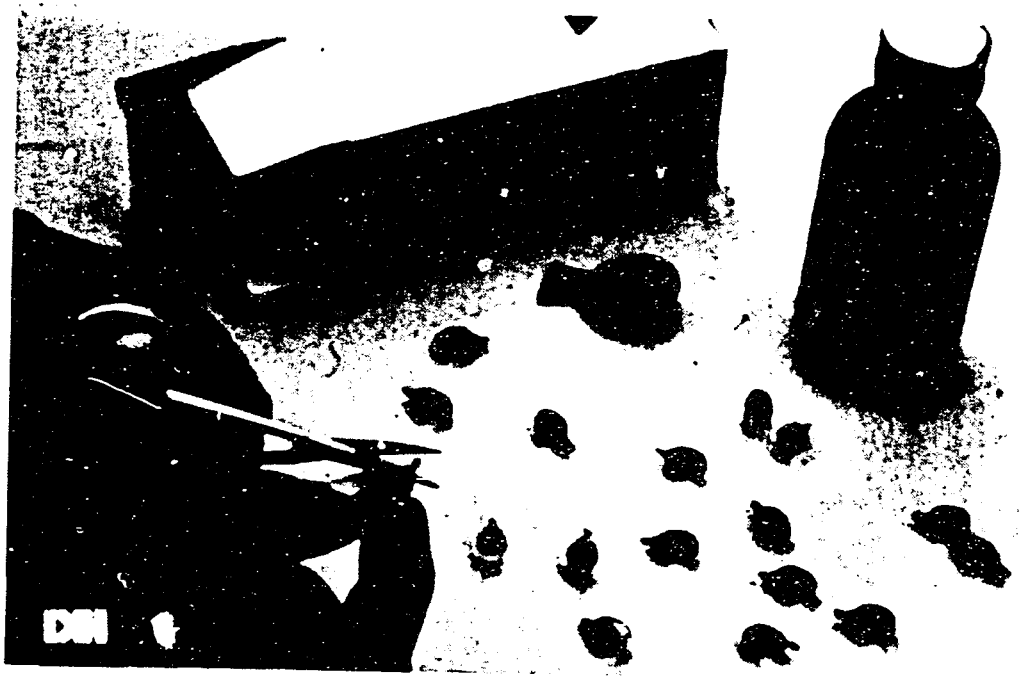
As the rash goes away, it leaves stains on the skin.

The skin often begins to peel.

Vitamin A Schedule

	Immediately on diagnosis	Following Day
Infants 6-11 months or < 8 kg.	100,000 IU	100,000 IU
Children one year and older	200,000 IU	200,000 IU

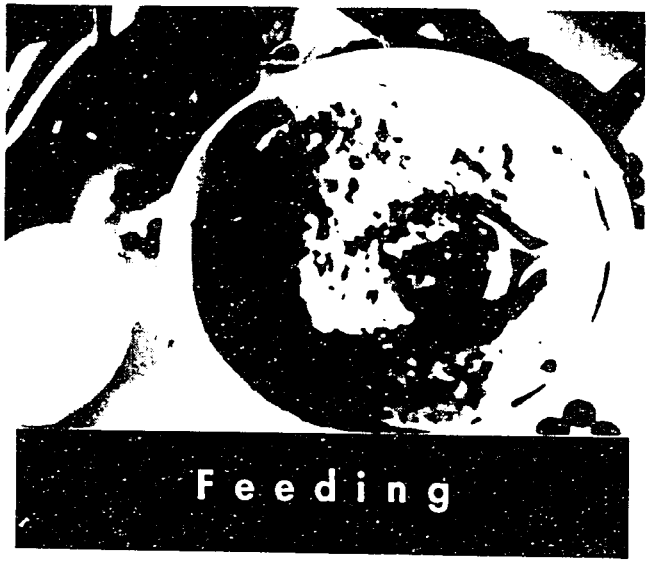
Dosing with Vitamin A



Vitamin A Supplies

- No refrigeration but store in a cool and dry place
- Do not freeze
- Keep out of direct sunlight, covered, in a dark place
- Use opened bottles and packages first

Feeding and Fluids are Critical



- "More fluids to prevent dehydration"
- "More food, more variety, more often"
- "Prevent weight loss"

Nutrition Messages

- **0-5 months: Breastfeed more often**
- **6+ months: Breastfeed, plus,**
  - **— extra protein foods**
    (animal foods, dairy products, dried beans, nuts)
  - **— extra energy foods**
    (oil, butter, sugar)
  - **— extra fruits and vegetables**
    (mango, squash, spinach/other dark green leaves)
- **All ages:**
  - **— plenty of fluids**
  - **— monthly or weekly weighing**

Complications

- **Fever:** Paracetamol when > 39^0 C, sponge with cool water.
- **Malnutrition:** Breastfeed, feed frequently, add sugar/ oil/ milk to weaning foods, monitor weight
- **Otitis Media:** Clean out discharge, give oral antibiotic (amoxycillin or ampicillin)

continued...

Pneumonia, Stridor/Croup

- **Cause:** measles virus or secondary bacterial or viral infections
- **Diagnosis:** cough and fast breathing
- **Treatment:** oral antibiotic – cotrimoxazole or amoxycillin
- **Severe pneumonia:** chest indrawing (stridor/croup) in addition to fast breathing

Admit children with severe pneumonia to the hospital

Eye Lesions

- **Diagnosis:**
  - — red eyes (conjunctivitis)
  - — inflammation of the cornea (keratitis)
  - — pain, opacity (corneal lesions)
- **Treatment:** antibiotic eye ointment for bacterial conjunctivitis.
- **If cornea is affected:** give a third dose of vitamin A 4 weeks after the second dose

Diarrhea/Dehydration

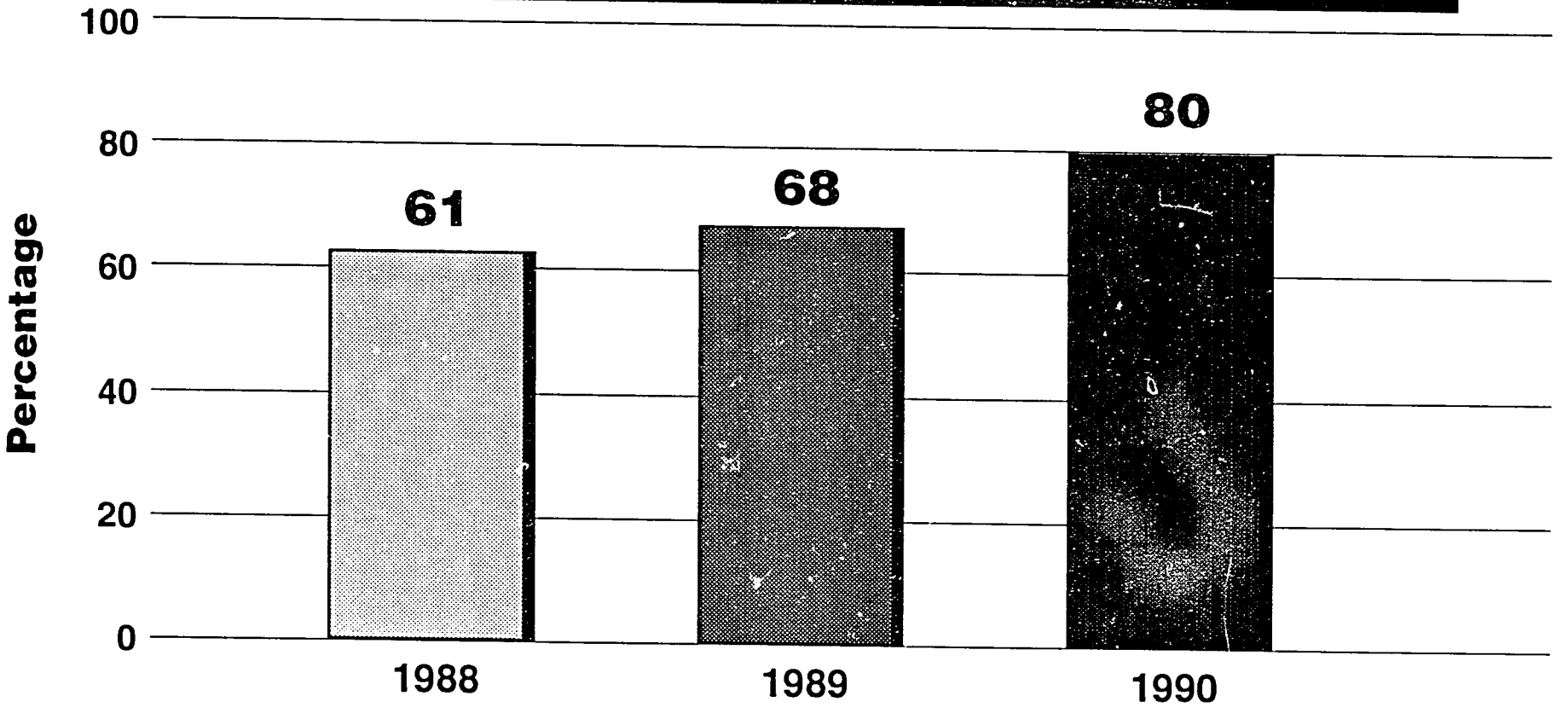
- **Dehydration signs:** dry mucous membranes, loss of skin elasticity, thirst
- **Mild – moderate dehydration:** use oral rehydration therapy (ORT)
- **Severe dehydration:** intravenous fluids
- **Bloody stools (dysentery):** antibiotics

Supplies Needed

Paracetamol	Tabs 100 mg
Vitamin A	Caps 200,000 IU
Cotrimoxazole	Tabs 80 mg
Amoxycillin	Caps 250 mg
ORS (oral rehydration salts)	Sachet for 1 litre
Tetracycline	Eye ointment 1% tube 5g

Immunization

Global Coverage with Measles Vaccine



VITAL

Expanding Coverage

- Immunize as soon as possible after 9 months
- Can be given at the same time as other EPI vaccines
- Unless there is documented evidence of prior immunization, immunize every eligible child
- Enlist the help of local leaders
- Use special campaigns when routine coverage remains low

Targets for 1995

World Summit for Children (Declaration, 1990)

"Reduction by 95 per cent in measles deaths and reduction by 90 per cent of measles cases."

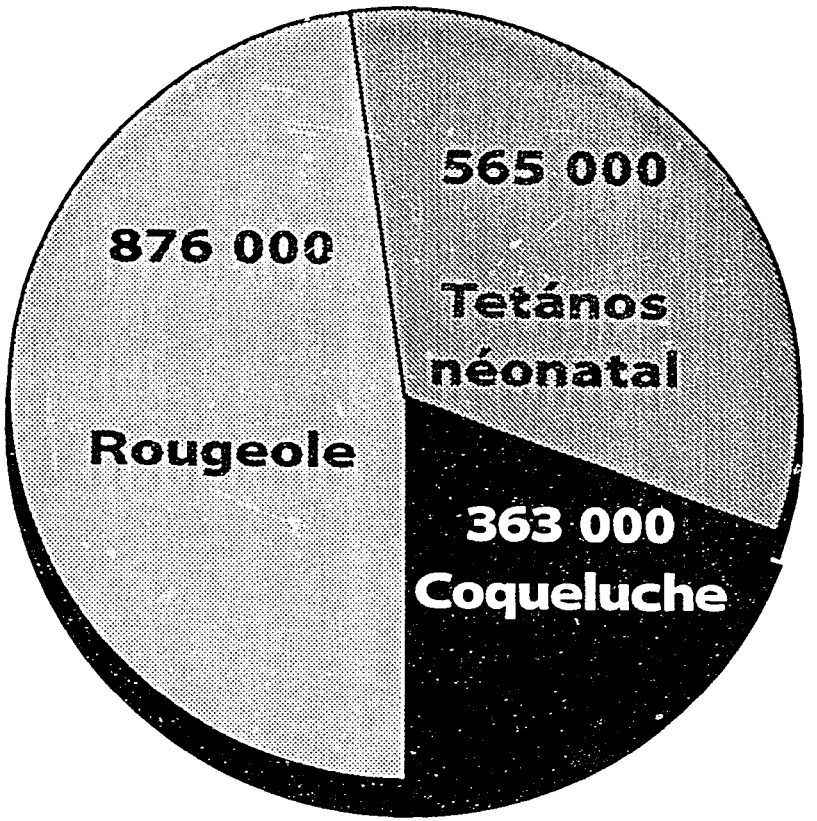
Strategy

- Effective Case Management Including Vitamin A
- Universal Immunization

vital: diaporama

Rougeole et vitamine A

Causes de la mortalité infanto-juvénile



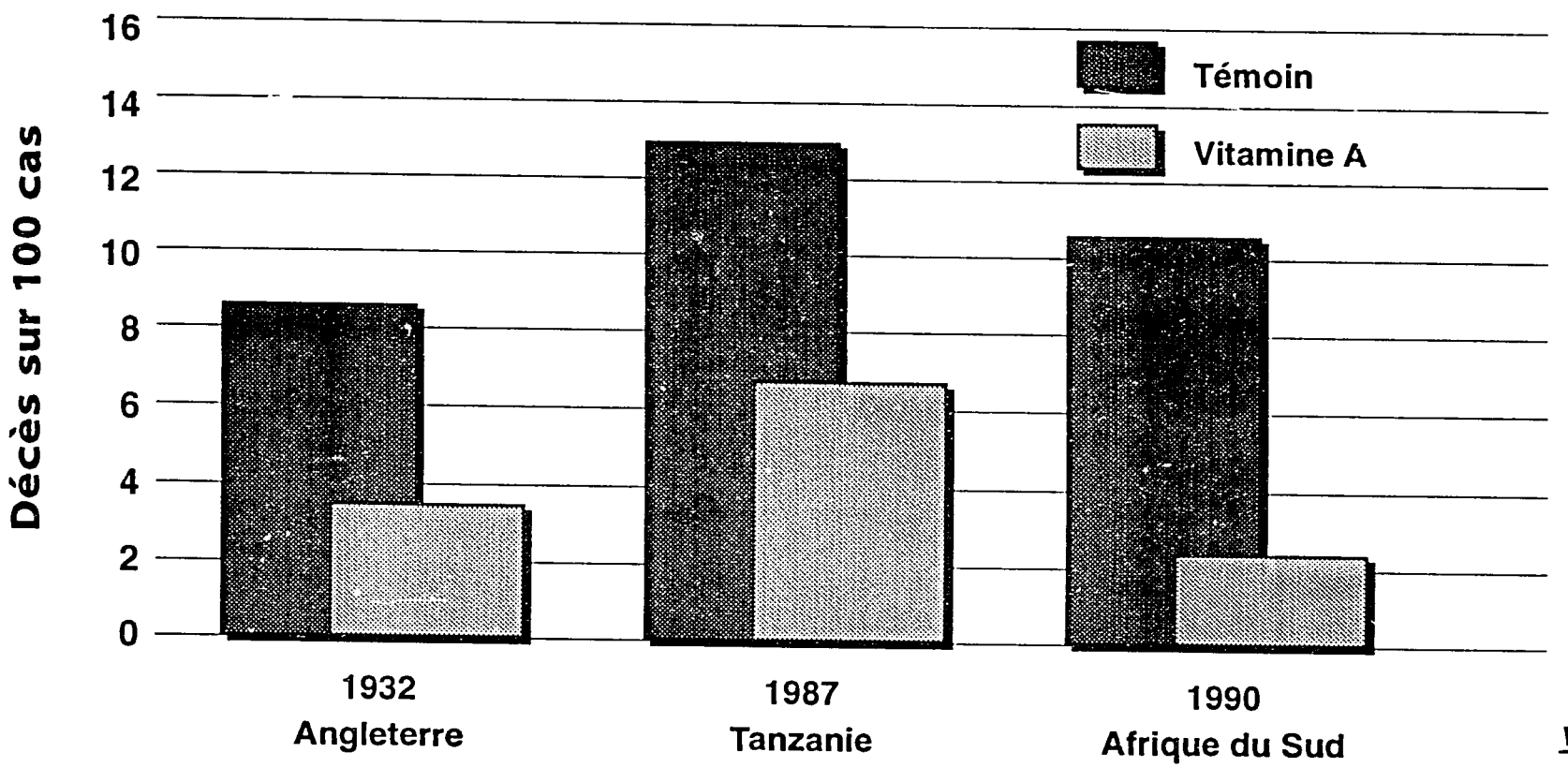
Estimation de la mortalité attribueé aux maladies cibleés par le PEV (1991)

Conséquences de la rougeole

- **Décès** ← pneumonie, diarrhée, croup, autres infections
- **Infirmités** ← cécité, autite moyenne, encéphalite
- **Retard de croissance** ← malnutrition

Effet de la vitamine A

● Rougeole → Cécité ● Rougeole..... ↓ Rétinol sérique



VITAL

La rougeole et la vitamine A

Manifestations chez les rougeoleux.....

- Vitamine A sérique ↓
- Réactions immunitaires ↓
- Epithélium affaibli, invasion d'agents pathogènes
- Diarrhée grave, infections respiratoires aiguës, lésions de la cornée

La vitamine A par voie orale augmente les niveaux de rétinol sérique et limite les lésions oculaires, les complications et les déces

VITAL

Prise en charge

- Diagnostic de la rougeole
- Suppléments de vitamine A
- Conseils á la mère
- Vérification de la situation vaccionale de l'enfant
- Diagnostic des complications
- Traitement des complications

Est-ce que c'est la rougeole?

Jour A a 3

L'enfant a froid, il tousse et a un peu de fievre. Les yeux sont rouges, mouillés et sensibles a la lumiere

Une éruption apparait sur le front

Une éruption apparait derriere les oreilles

Jour 3 a 4

Les yeux sont rouges et couverts d'un liquide jaune collant

L'éruption couvre le visage

L'éruption se repand sur tout le corps

Jour 4 a 6

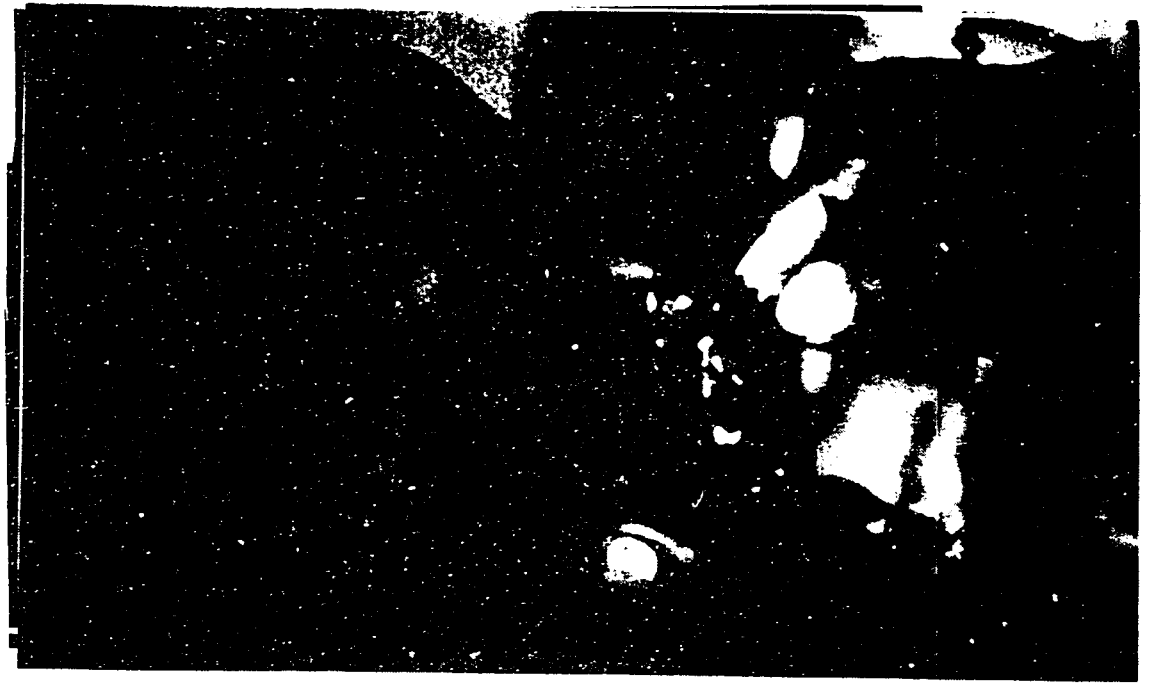
Au fur et a mesure qu elle desparait, l'éruption paisse des taches sur la peau. La peau commence souvent a s'ecailler

Quand et comment administrer la vitamine A?

	Dès le diagnostic	Lendemain
Infants 6-11 mois ou < 8 kg.	100 000 IU	100 000 IU
Enfants d'un an et plus	200 000 IU	200 000 IU

9

Suppléments de vitamina A



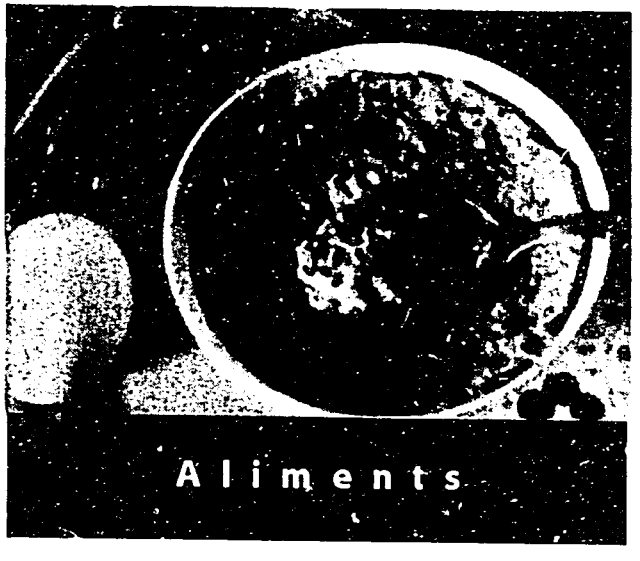
VITAL

L'approvisionnement en vitamine A

- Pas de refrigération nécessaire. Placer les produits au frais et au sec
- Ne pas congeler
- Ne pas exposer les produits à la lumière du soleil, les conserver couverts dans un lieu sombre
- Utiliser d'abord les flacons et les boîtes entamés

Il est essentiel de boire et de manger

- "Boire davantage pour prévenir la déshydratation"



- "Manger davantage plus varié et plus frequemment"

- "Prévenir les pertes pondérales"

VITAL

Conseils de nutrition

- **0-5 mois: allaiter plus souvent**
- **6 mois et plus: allaiter et en plus**
  - **ajouter des aliments à forte teneur protéique** (viandes, produits laitiers, haricots secs, fruits à écale)
  - **ajouter des aliments à forte teneur énergétique** (huile, beurre, sucre)
  - **ajouter des fruits et des légumes** (mangue, courge, épinards et autres feuilles vertes)
- **Tout âge:**
  - **Beaucoup de liquides**
  - **Pesage hebdomadaire ou mensuel**

Complications

- **Fièvre:** Paracétamol quand > 39^0 C, compresses d'eau froide.
- **Malnutrition:** Nourrir au sein, donner à manger souvent, ajouter sucre/huile/lait aux aliments de sevrage, suivre le poids.
- **Autite moyenne:** nettoyer les sécrétions, donner des antibiotiques oraux (amoxycilline ou ampicilline)

continued...

Pneumonie, strideur/croup

- **Cause:** virus de la rougeole ou infections bactériennes ou virales secondaires
- **Diagnostic:** toux et respiration rapide
- **Traitement:** antibiotiques oraux-cotrimoxazole ou amoxycilline
- **Pneumonie aiguë:** tirage (croup) en plus de la respiration rapide.

Hospitaliser les enfants souffrant de pneumonie aiguë

Lésions oculaires

- **Diagnostic:**

  — yeux rouges (conjonctivite)

  — inflammation de la cornée (kératite)

  — douleur, opacité (lésions cornéennes)

- **Traitement:** collyres antibiotiques pour traiter la conjonctivite bactérienne.

- **Si la cornée est affectée:** administrer une troisième dose de vitamine A 4 semaines après la deuxième dose.

Diarrhée/déshydratation

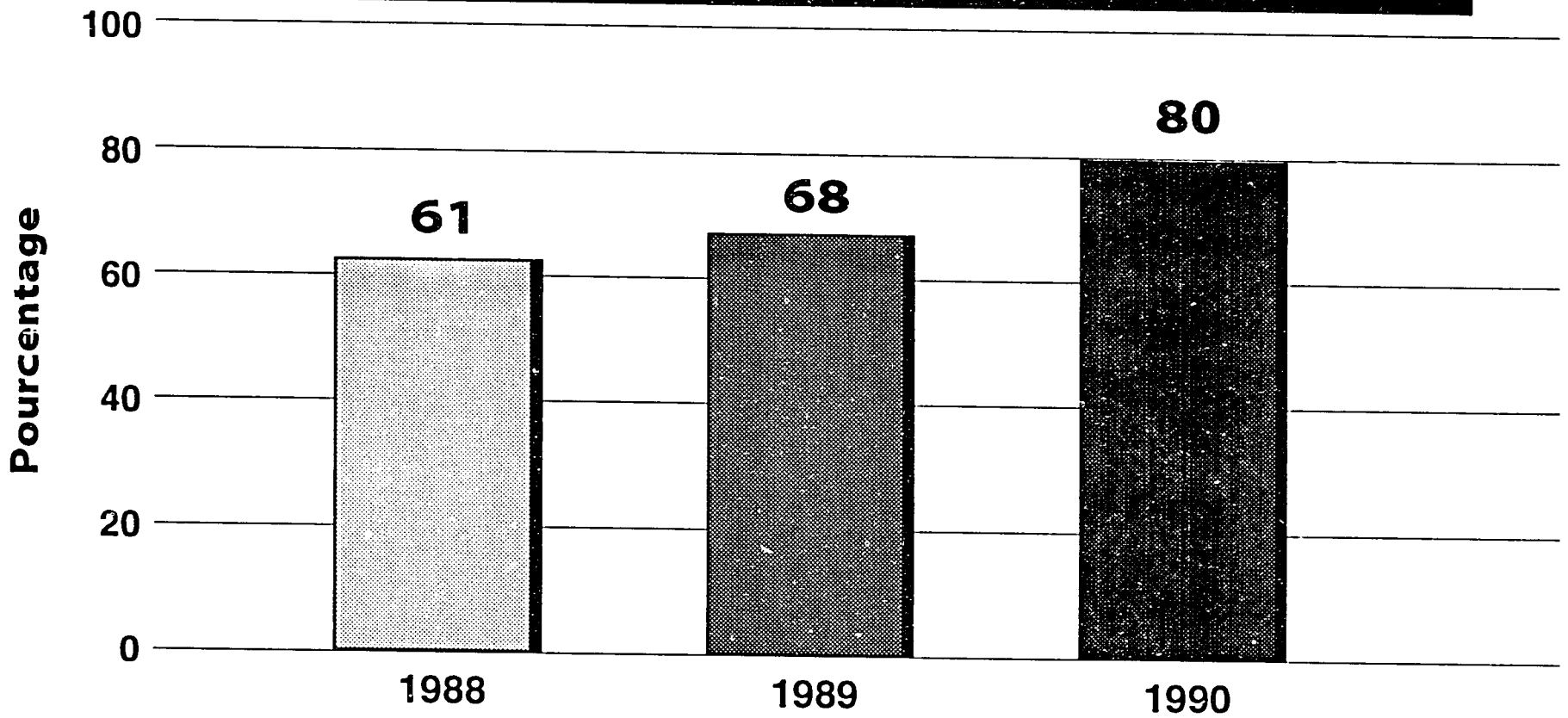
- **Signes de déshydratation:** membranes muqueuses sèches, perte d'élasticité de la peau, soif.
- **Déshydratation modérée:** employer la thérapie de réhydratation orale (TRO)
- **Déshydratation aiguë:** administration des fluides par voie intraveineuse.
- **Sang dans les selles (dysenterie):** antibiotiques.

Produits nécessaires

Paracétamol	Cachets 100 mg
Vitamine A	Capsules 200 000 et 100 000 IU
Cotrimoxazole	Cachets 80 mg
Amoxycilline	Capsules 250 m
SRO (sels de réhydratation orale)	Sachet pour 1 litre
Tétracycline	Pommade 1% tube 5 g

Vaccination

Couverture globale du vaccin anti-rougeoleux



VITAL

Augmentation de la couverture vaccinale

- Vacciner dès que possible après le 9e mois.
- Vaccin peut être administré en même temps que les autres vaccins du PEV.
- A moins qu'il apparaisse clairement que les sujets ont été vaccinés, vacciner tous les enfants devant l'être.
- Faire appel à l'aide de dirigeants locaux.
- Mettre en oeuvre des campagnes spéciales lorsque la couverture est insuffisante.

Objectifs pour 1995

Sommet Mondial pour les Enfants (Declaration de 1990)

"Réduction de 95% de la mortalité attribuable à la rougeole et réduction de 90% des cas de rougeole."

Stratégie

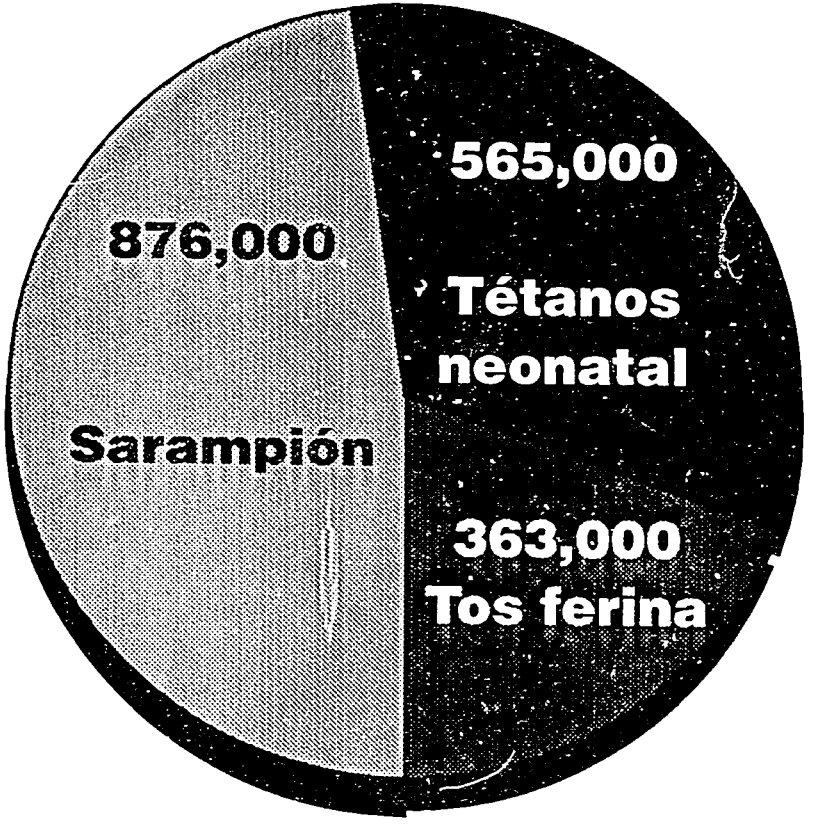
- Prise en charge efficace y compris vitamine A
- Vaccination universelle

presentación de diapositivas vital

Sarampión y vitamina A

2

Causas de mortalidad infantil



Muertes estimadas por enfermedades prevenibles por inmunización (1991)

VITAL

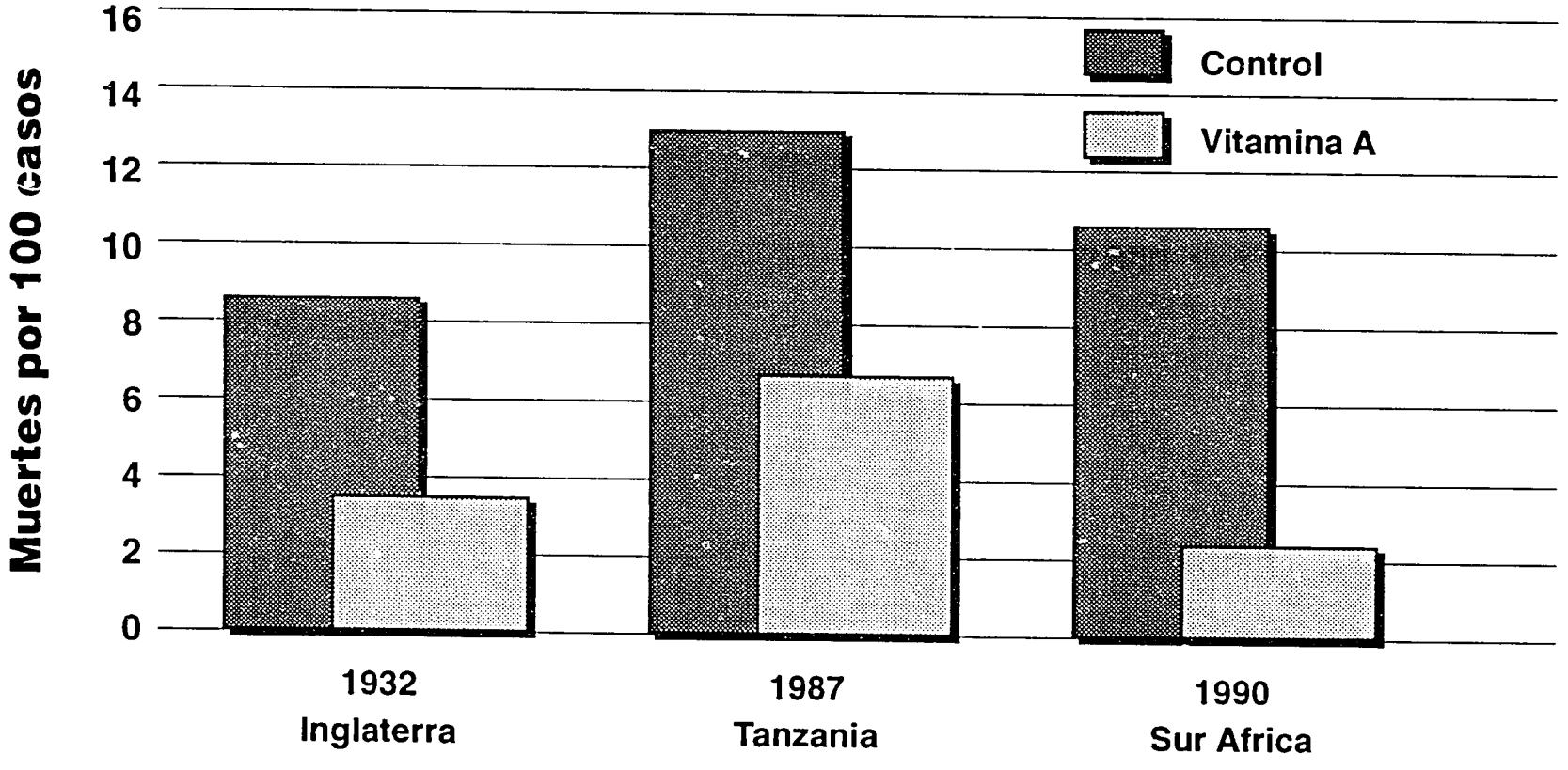
Consecuencias del sarampión

- **Muertes** ← neumonía, diarrea, crup, otras infecciones
- **Incapacidad** ← ceguera, otitis media, encefalitis
- **Retraso en el crecimiento** ← desnutrición

4

Impacto de la vitamina A

● Sarampión → Ceguera ● Sarampión ↓ Retinol sérico



VITAL

El sarampión y la vitamina A

En pacientes con sarampión.....

- Vitamina A sérica ↓
- Reacciones inmunológicas ↓
- Epitelio debilitado, invasión de patógenos
- Diarrea severa, IRA, daño a la córnea

La vitamina A por vía oral incrementa los niveles de retinol sérico y limita el daño del ojo, las complicaciones, y las muertes.

Manejo de las casos

- Diagnóstico del sarampión
- Dosificación de la vitamina A
- Consejos a la madre
- Preguntas sobre las vacunas
- Diagnóstico de las complicaciones
- Tratamiento de las complicaciones

¿Es sarampión?

Días 1-3

El nino está resfriado y tiene tos y fiebre.

Los ojos estàn rojos y húmidos y muy sensibles a la luz.

Aparece un brote en las frente y detras de las orejas.

Días 3-4

Los ojos están rojos y cubiertos de un liquido pegajoso amarillento.

El brote cubre la cara y se extiende por todo el cuerpo.

Días 4-6

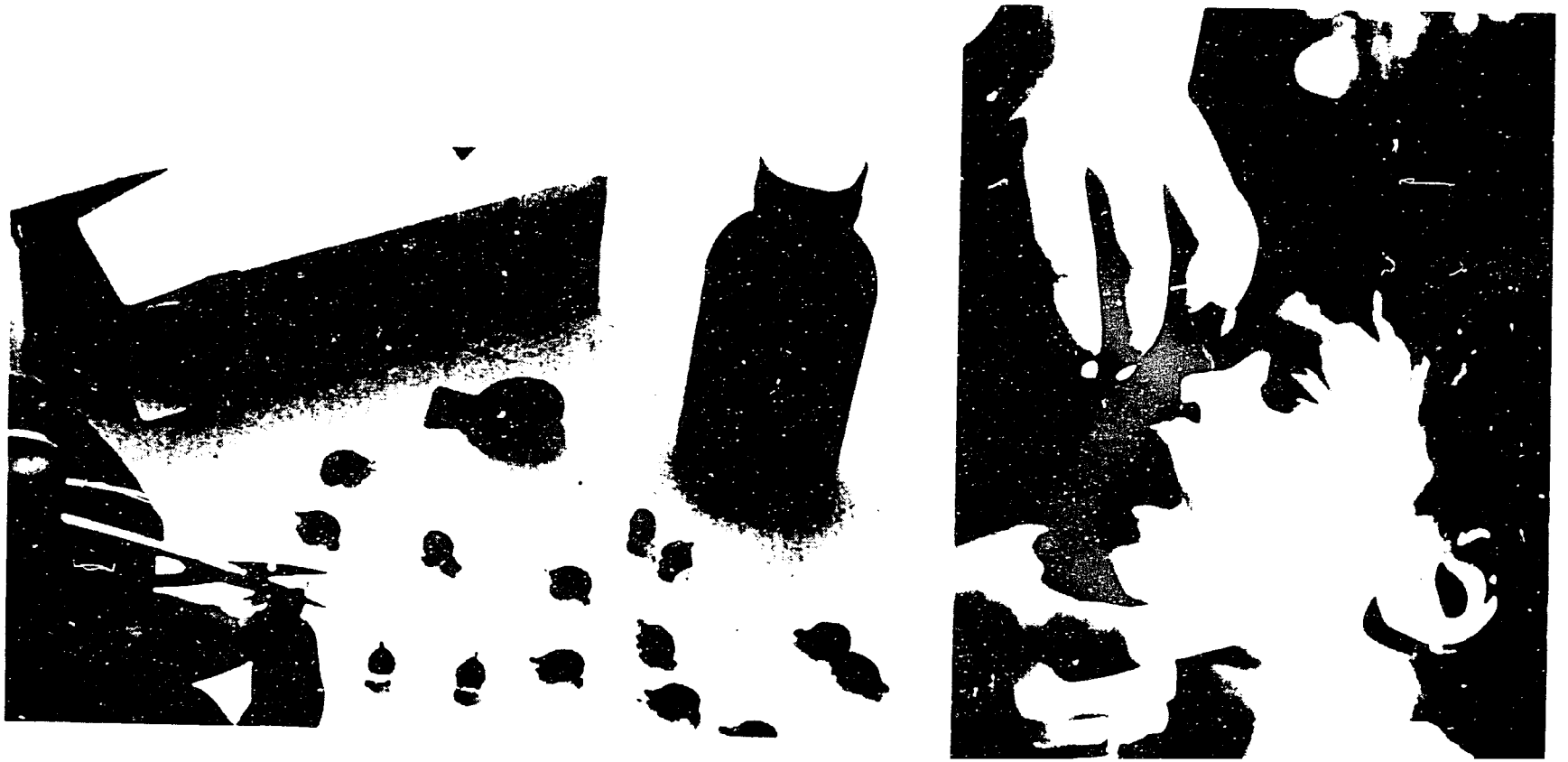
A medida que el brote desaparece deja manchas en la piel.

Con frecuencia la piel comienza a descamarse.

Plan de tratamiento con vitamina A

	Al diagnóstico	Al día siguiente
Niños de 6 a 11 meses o < 8 kg.	100.000 UI	100.000 UI
Niños de 1 año o mayores	200.000 UI	200.000 UI

Dosificación de la vitamina A



Provisiones de vitamina A

- No se necesita refrigeración pero debe guardarse en un lugar fresco y seco
- No la congele
- Mantengala fuera de la luz del sol, cubierta en un lugar oscuro
- Utilize primero los paquetes y frascos ya destapados

La Alimentación y los líquidos son críticos

- "Más líquidos para prevenir la deshidratación"

- "Más comida, más variedad, con mayor frecuencia"

- "Previene la pérdida de peso"

Mensajes nutricionales

- **0-5 meses: lactancia más frecuente**
- **6+ meses: lactancia, más**
  - **alimentos proteínicos adicionales** (alimentos animales, productos lácteos, frijoles secos, nueces)
  - **alimentos energéticos adicionales** (aceite, mantequilla, azúcar)
  - **frutas y vegetales adicionales** (mango, ahuyama, espinaca/otras hortalizas de hojas verde oscuro)
- **Para todas las edades:**
  - **suficientes líquidos**
  - **control de peso semanal o mensual**

Complicaciones

- **Fiebre:** Paracetamol cuando la temperatura es > 39^0 C, esponja (o toalla) con aqua fría.

- **Desnutrición:** Lactancia materna, alimentación frecuente, agregar azúcar, aceite o leche a los alimentos del destete, vigilar el crecimiento

- **Otitis media:** Limpie las secreciones, dé antibioticos orales (amoxicilina o ampicilina)

continúa...

Neumonía, Crup

- **Causa:** virus del saramión o infecciones secundarias bacterianas o virales.
- **Diagnóstico:** tos y respiración rápida
- **Tratamiento:** antibiótico oral – cotrimoxazol o amoxicilina.
- **Neumonía severa:** tiraje (crup) además de respiración rápida

Hospitalize a los niños con neumonía severa

Lesiones oculares

- **Diagnóstico:**
  - — ojos rojos (conjuntivitis)
  - — inflamación de la córnea (keratitis)
  - — dolor, opacidad (lesiones de la córnea)
- **Tratamiento:** unguento oftálmico de antibióticos para la conjuntivitis bacteriana.
- **Si la córnea está afectada:** administre una tercera dosis de vitamina A 4 semanas después de la segunda dosis.

Diarrea/Deshidratación

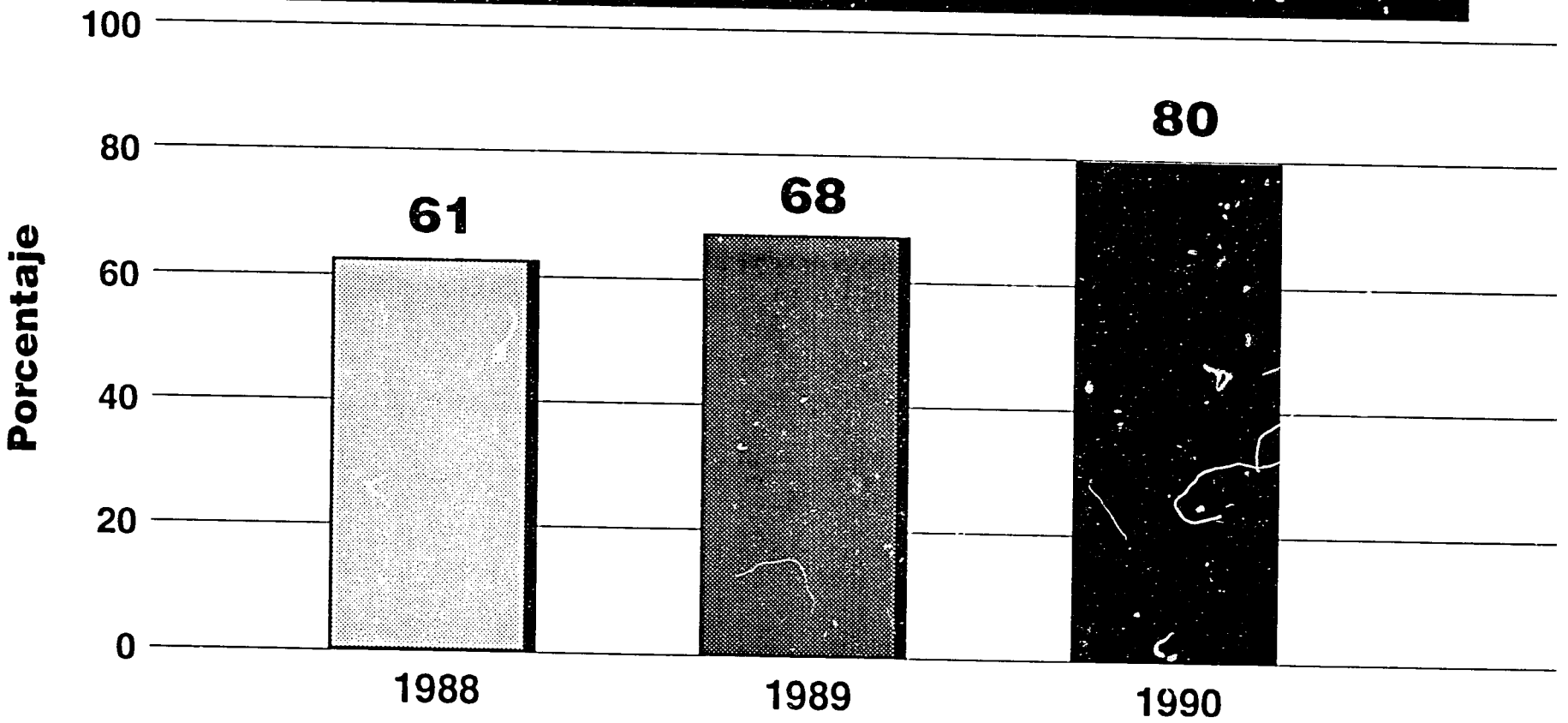
- **Signos de deshidratación:** membranas mucosas secas, pérdida de elasticidad de la piel, sed
- **Deshidratacíon leve a moderada:** utilize la terapia de rehidratacíon oral (TRO)
- **Deshidratación Severa:** rehidratación endovenosa
- **Deposiciones con sangre (disentería):** antibióticos

Materiales Necesarios

Paracetamol	Tabletas de 100 mg
Vitamina A	Cápsulas de 200.000 UI and 100.000 UI
Cotrimoxazol	Tabletas de 80 mg
Amoxicilina	Cápsulas de 250 mg
Sales de rehidratación oral	Paquetes o sobres para 1 litro
Tetraciclina	Ungüento oftálmico al 1%, tubo de 5 g

Vacunación

Cobertura global de la vacuna contra el sarampión

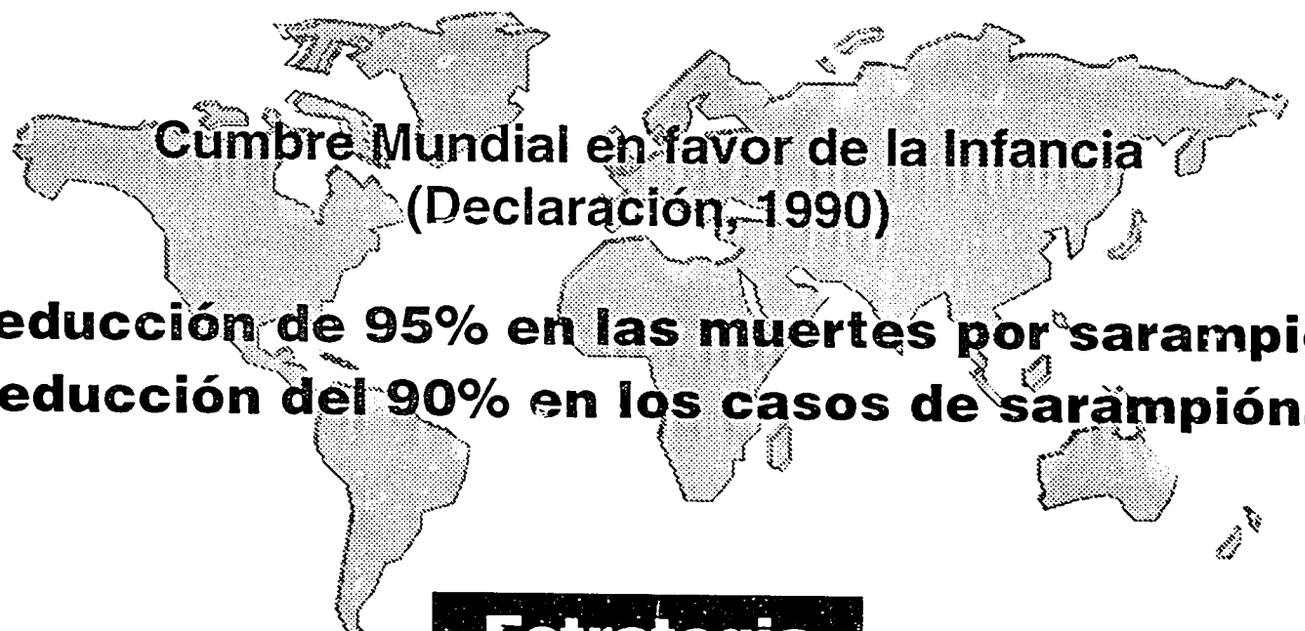


VITAL

Ampliación de la cobertura

- Vacunar lo más pronto posible después de los 9 meses
- Se puede administrar junto con otras vacunas del PAI
- A menos que se compruebe vacunación anterior, vacunar a todos los niños elegibles
- Asegurar la colaboración de los líderes locales
- Usar campañas especiales cuando la cobertura de rutina se mantiene baja

Metas para 1995



Cumbre Mundial en favor de la Infancia
(Declaración, 1990)

"Reducción de 95% en las muertes por sarampión y reducción del 90% en los casos de sarampión."

Estrategia

- Manejo efectivo de los casos, incluyendo el uso de vitamina A
- Vacunación universal

Vitamin A supplementation reduces measles morbidity in young African children: a randomized, placebo-controlled, double-blind trial[1-3]

Anna Coutsoudis, Michael Broughton, and Hoosen M Coovadia

ABSTRACT The effects of vitamin A supplementation on measles morbidity are unclear. Sixty hospitalized children aged 4–24 mo with complicated measles received a World Health Organization–(WHO) recommended dose of vitamin A or placebo. The two groups were comparable in known covariants of measles severity: weight-for-age percentiles, overcrowding, rash, total lymphocytes, and serum concentrations of zinc, albumin, prealbumin, retinol-binding protein, and vitamins A and E. Ninety percent of the patients had hyporetinemia. Integrated morbidity scores, determined by severity of condition (eg, diarrhoea, herpes, and respiratory-tract infection) were assigned on day 8 and 6 wk and 6 mo; these were reduced by 82%, 61%, and 85%, respectively, in the supplemented group, which was mainly due to reduced respiratory-tract infection. There was one death in the placebo group. At 6 wk weight gain was significant in the supplemented group. Despite the selected sample, attention to multiple covariates enhances the validity of the data obtained and supports the current WHO recommendations for vitamin A supplementation during measles. *Am J Clin Nutr* 1991;54:890–5.

KEY WORDS Measles, vitamin A supplementation, morbidity

Introduction

Vitamin A deficiency, recognized for its ocular complications, has been shown to have systemic effects that increase mortality (1) and morbidity (2, 3). There is some evidence that this effect on mortality may be reversed by supplementation (4, 5). The results of some intervention studies are unfortunately clouded by design and measurement problems (6, 7). Serum retinol concentrations are reduced during measles (8–10) and may be partly responsible for increased mortality from the disease (11). Suggestive, though inconclusive, evidence indicates that measles mortality may be reduced by vitamin A supplementation (12, 13). On the basis of this evidence the World Health Organization (WHO) recommends that in areas where the measles fatality rate is > 1%, children with measles should be supplemented with vitamin A (14).

Because measles remains one of the most severe infectious diseases in children in poor communities (15), there are profound public health implications in such a policy. However, there is no good evidence that morbidity can be reduced by vitamin A supplementation during measles infection. A major factor that will affect the strength of any vitamin A–intervention trial is comparability between the vitamin A–treated and control groups, because demographic, nutritional, immunological, and clinical indices affect outcome (16, 17). A criticism of previous studies has been an imprecise recording of morbidity data, in particular, little assessment of the severity of respiratory infections (7).

The detrimental effects of severe measles are maximum within 3 mo but may be evident for up to 6 mo (9) or even 1 y (18) after the acute attack; therefore, any trial designed to assess the effects of vitamin A supplementation on measles should include follow-up of the children. We report the findings of a random, double-blind, placebo-controlled vitamin A intervention trial, which paid particular attention to many of the known covariants of measles severity and vitamin A status and in which children were followed for 6 wk to 6 mo.

Subjects and methods

Subjects

Sixty African children (aged 4–24 mo) of poor socioeconomic background, presenting at Durban's King Edward VIII Hospital (KEH) with measles complicated by pneumonia and diarrhea severe enough to warrant admission to the Fevers Hospital (Clairwood Hospital), were studied. The diagnosis of measles was made on clinical grounds. Dietary and socioeconomic information was obtained from the mother or guardian after the child was entered into the trial. The premeasles vitamin A status of our patients was unclear because there are no good data in South Africa on the prevalence of vitamin A deficiency, but

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reports suggest that xerophthalmia is most often detected in association with protein-energy malnutrition (19, 20) and that there also appears to be a moderate to high prevalence of subclinical deficiency in some rural African communities (21). Patients were admitted to the trial on weekday mornings between April and October 1989.

Written informed consent was obtained from the parent or guardian before a child was admitted to the trial. The study protocol was approved by the University of Natal Medical Faculty's Ethics and Research Committee.

Children aged > 24 mo, with a rash for > 5 d, and those who had received vitamin supplements in the month before admission were excluded from the trial. Children who did not have both pneumonia and diarrhea complications were excluded as were any children with laryngotracheobronchitis (LTB). Restriction of the trial to those aged < 24 mo was because this age group is at greatest risk for morbidity and mortality and that this infection is most common in children aged 4–24 mo in the Third World (22). It was decided that any child with clinical signs of vitamin A deficiency would be treated with vitamin A and would be excluded from entry into the trial. At completion of the study it was noted that no child had been excluded for this reason.

Methods

Both groups received standard therapy (antibiotics, antipyretics, and oral rehydration) and monitoring for measles and its complications. The trial group received vitamin A (retinyl palmitate, Arovit Drops, Roche Products, Isando, South Africa) either 54.5 mg (< 12 mo) or 109 mg (≥ 12 mo). The control group received a placebo syrup. Vitamin A or placebo was administered by the same person (AC) on admission and on days 2 and 8. The dose of vitamin A given to the experimental group was the amount recommended by the WHO (14).

The assumption used in determining sample size was that the recovery rate (within 7 d) from complicated measles under standard treatment is 50%. Assuming that with vitamin A supplementation 80% of the patients would recover within 7 d, and choosing an α error of 0.05% and a β error of 0.5%, we estimated that we needed 29 patients in each group to detect an absolute increase in recovery of 30%. The patients were allocated to treatment or placebo groups according to a table of random numbers. The treatment- and placebo-dropper bottles were number coded.

Apart from vitamin A status many other factors have been suggested as determinants of severity of measles. We therefore recorded values of these other factors to ensure that when the code was broken the comparability of the two groups could be considered. These factors were lymphocyte count $< 2 \times 10^9$/L (23), objective analysis of extent of pneumonia on chest radiograph (CXR) (23), amount of serum complement (C_3) (17), protein-energy malnutrition determined by weight-for-age percentiles according to the National Center for Health Statistics (NCHS), clinical features and serum albumin concentrations, extent of rash (24), and degree of overcrowding at home (25). Information was taken from the child's parent or guardian to derive an overcrowding index (number of persons/number of rooms), which Aaby et al (16) suggested is an even more important index of severity than is poor nutrition. A higher overcrowding index could, however, also be associated with decreased vitamin A intake (26). Rash was graded according to the following: face = 1, 1 + trunk = 2, 2 + limbs = 3.

The CXR score was determined by AW, who was unaware of the treatment groups. The severity of the abnormalities in the lung fields was graded by awarding points for areas of patchy consolidation to a maximum of four; one point being given for each of the following: atelectasis; involvement of the peripheral lung fields, either by emphysema or consolidation; and effusion. Each child was given a score from 0 to 7 for their CXR at days 1 and 42 and at 6 mo. A score > 3 was considered as an index for severe measles. We successfully used many of these criteria over the last 15 y to assess severity (23).

Vitamin A is stored in the liver but is dependent on retinol-binding protein (RBP) for mobilization into the plasma, where it travels as an RBP complex in association with prealbumin to target tissues. RBP synthesis appears to be dependent on zinc concentrations (27); we therefore determined zinc, RBP, and prealbumin concentrations. Because there appears to be an interaction between vitamins A and E (28), we determined vitamin E concentrations simultaneously with vitamin A concentrations.

Patients were followed daily in the hospital and were assessed for duration of fever, diarrhea (≥ 3 loose or watery stools a day), and pneumonia (presence of tachypnea with retractions, crackles, or wheezes and other less-common complications). Incidences of herpes stomatitis and LTB were recorded. Complete clinical recovery was the stage at which fever, diarrhea, pneumonia, and other complications were clinically resolved.

On discharge each mother was given a plastic laminated appointment card requesting her to bring the child to KEH for a follow-up appointment on day 42. The card had space for the mother to record any illnesses the child might have had in the interim between hospital discharge and the follow-up appointment. The mother was also told to carry this card with her if she ever took the child to a clinic so that the clinic diagnosis could be recorded. Incentives were provided to encourage follow-up. At the 6-wk appointment the children were given another dose of vitamin A or placebo and were given a date for a 6-mo follow-up appointment. At the 6-wk and 6-mo follow-up appointments the child had a CXR taken and a full clinical examination done by the same pediatrician (MB).

An integrated morbidity score (IMS) was calculated for each child based on the following rating system: 0–4 for diarrhea, upper respiratory-tract infection (URTI), pneumonia, and LTB where 0 is not present, 1 is reported by mother or guardian, 2 is documented mild condition, 3 is a documented severe condition not requiring hospitalization, and 4 is a condition requiring hospitalization. (For pneumonia and LTB the rating system is weighted by a factor of 2 for the 6-wk and 6-mo IMS.); 0–2 for herpes, where 0 is absent, 1 is localized, and 2 is disseminated; and 3–7 for CXR rating. Each child was assigned a score on days 1 and 8 and immediately after the 6-wk and 6-mo appointment, before the code was broken.

On admission to the trial a blood sample was taken by venipuncture before any vitamin A or placebo was administered. Serum was separated within 5 h and 3-μL portions were stored in microcentrifuge tubes at −70 °C until analyzed for zinc, albumin, prealbumin, RBP, and vitamins A and E. Serum was stored between 1 and 10 mo before analysis. During all procedures blood samples were protected from sunlight to prevent photodestruction of vitamin A. Approximately equal numbers of placebo and treated patients were analyzed in the same run

TABLE 1
Baseline characteristics of children with measles, by treatment group*

	Placebo (n = 13 M, 18 F)	Vitamin A (n = 16 M, 13 F)
Age (mo)	10.42 ± 0.70†	12.17 ± 1.00
Wt/age <80% of standard‡	9	9
CXR score > 3	5	7
Lymphocytes <2 × 10^9/L	6	4
Lymphocytes <2 × 10^9/L and CXR score > 3	1	2
C_3 (g/L)	1.02 ± 0.03	1.14 ± 0.06
Overcrowding index§	2.68 ± 0.44	2.65 ± 0.35
Rash grade‖	2.13 ± 0.12	2.00 ± 0.12
IMS	9.82 ± 1.80	10.56 ± 1.96

* There were no significant differences between the groups for any of the characteristics.
† $\bar{x}$ ± SE.
‡ 50th National Center for Health Statistics percentile; no child had clinical features of protein-energy malnutrition.
§ Number of persons per room.
‖ 1 = face; 2 = face, trunk; 3 = face, trunk, limbs.

TABLE 2
Baseline hematological and serum micronutrient concentrations in children with measles, by treatment group*

	Placebo (n = 31)	Vitamin A (n = 29)
Hemoglobin (g/L)	110.5 ± 3.5	108.6 ± 3.1
Lymphocytes (×10^9/L)	3.80 ± 0.42	3.70 ± 0.37
Albumin (g/L)	31.84 ± 0.65	30.10 ± 1.05
Zinc (μmol/L)	13.46 ± 0.43	12.55 ± 0.43
Prealbumin (mg/L)	92.6 ± 7.0	94.5 ± 4.6
Retinol-binding protein (mg/L)	14.6 ± 1.4	14.9 ± 1.2
Vitamin A (μmol/L)	0.41 ± 0.04	0.43 ± 0.04
Vitamin E (mg/L)	4.9 ± 0.4	4.9 ± 0.4

* $\bar{x}$ ± SE. There were no significant differences between the groups for any of the investigations.

and plate. All analyses were done in duplicate and a CV of > 5% between duplicates resulted in the analysis being repeated.

Vitamin A (as retinol) and vitamin E (as α-tocophertol) were simultaneously measured by normal phase HPLC by using fluorescence detection. The method used was a modification of a previously reported method (29). We used an HP 1090 HPLC instrument (Hewlett-Packard, Waldbronn, FRG) attached to a programmable flourescence detector (HP 1046A). The column used was a normal phase microbore column (spherisorb S3W, Phase Sep, Queensferry, Wales, UK). Zinc was measured by atomic-absorption spectrophotometry (AA-1275 series, Varian Techtron, Melbourne, Australia). Albumin and prealbumin were determined by laser nephelometry in the biochemistry laboratory at KEH. RBP concentrations were determined by commercially available radial immunodiffusion kits, LC-Partigen Plates (Behringwerke AG, Marburg, FRG). All the plates were from the same batch (lot no. 057325B). Full and differential blood counts were carried out in the routine KEH hematology laboratory.

Statistical methods

Differences in proportions in the data were examined by the chi-square test. Differences in the means were examined by Student's t test. The level of significance used was 5%. The software used for the computerized analysis of results was the *Statistical Analysis System* (*SAS*), release 6.03 edition, 1988 (SAS Institute Inc, Cary, NC).

Results

Baseline characteristics of the vitamin A and placebo groups were comparable. There were no significant differences between the two groups in any covariant considered (**Tables 1 and 2**).

Vitamin A–treated children recovered more rapidly from pneumonia ($\bar{x}$ ± SE 3.8 ± 0.40 vs 5.7 ± 0.79 d, $P < 0.05$), diarrhea, and fever than did the placebo group, although the latter two were not significantly different (**Table 3, Fig 1**). In addition, 28 of the 29 vitamin A–treated children (96%) recovered fully by clinical criteria within 7 d compared with 11 of the 31 placebo patients (65%), $P = 0.002$. The one death in the placebo group was due to pneumonia; he was lymphopenic on admission. The IMS on day 8 was significantly lower in the vitamin A group, representing an 82% reduction in the IMS.

The 6-wk follow-up was 80%. The 6-wk IMS was significantly lower in the vitamin A group than in the placebo group (**Table 4; Fig 1**). This 61% reduction in the IMS was mainly attributed to more severe episodes of pneumonia in the placebo group, as shown by the significantly higher pneumonia score per episode in the placebo group. Children in the supplemented group had gained significantly more weight over 6 wk than did the placebo group.

We had a poor 6-mo follow-up (60%) because of severe political unrest. The 6-mo IMS was significantly lower in the vitamin A group than in the placebo group (**Table 5; Fig 1**). The large reduction in the IMS (85%) in the supplemented group was attributed mainly to the increase in frequency and severity (as defined radiologically) of pneumonia episodes in placebo-

TABLE 3
Hospital morbidity outcome in children with measles, by treatment group

	Placebo (n = 31)	Vitamin A (n = 29)
Clinical-pneumonia duration (d)	5.7 ± 0.79*	3.8 ± 0.40†
Diarrhea duration (d)	4.5 ± 0.35	3.2 ± 0.71
Fever duration (d)	4.2 ± 0.50	3.6 ± 0.30
Herpes stomatitis	2 (6%)	3 (10%)
Laryngotracheobronchitis	1	0
Death	1	0
Complete clinical recovery in <8 d	20 (65%)	28 (96%)‡
IMS	1.37 ± 0.40	0.24 ± 0.15§

* $\bar{x}$ ± SE.
†‡§ Significantly different from placebo: †P = 0.037, ‡P = 0.002, §P = 0.006.

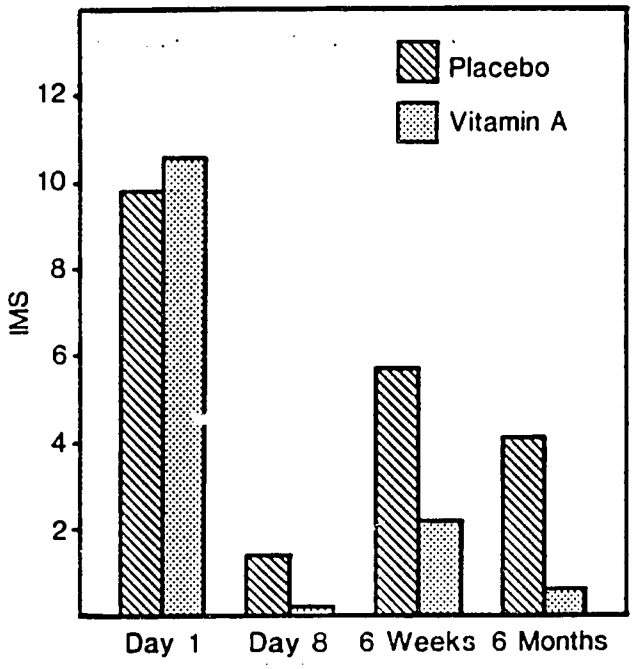

FIG 1. Integrated morbidity scores (IMS), by treatment group.

treated children. A significant difference in the number of URTI episodes also contributed to the overall poor morbidity of the placebo group.

Discussion

This study of hospitalized young African children from a community where xerophthalmia is uncommon, but where the children had reduced concentrations of serum retinol at onset of measles, demonstrated that supplementation with vitamin A within 5 d of the rash resulted in speedier recovery from pneumonia during the acute exanthematous phase and produced a significant reduction in the frequency and severity of postmeasles respiratory-tract complications. Additional vitamin A supplement on day 42 could have contributed to this significant reduction in morbidity, which was noted for ≤ 6 mo. The diminution of infectious morbidity rates probably accounted for the improved weight gain in the vitamin A–treated children during the 6 wk after the rash. Addition of vitamin A at baseline did not have any significant effect on the frequency or severity of diarrhea.

Although the prevalence of clinical signs of vitamin A deficiency in Durban appears to be low, our results confirm the findings of other workers that serum retinol concentrations are lowered during measles (8–10). We found hyporetinemia (serum retinol < 0.70 μmol/L) (30) in 90% of the patients. Both groups, however, had a marked increase in serum retinol concentrations on day 8, with the supplemented group having significantly higher concentrations than the placebo group (31). This finding would imply that the liver stores of these patients were not exhausted, except that there was a temporary impaired mobilization of vitamin A and increased tissue utilization of vitamin A. This effect of a temporary lowering of serum retinol could be especially

TABLE 4
Six-week morbidity outcome in children with measles, by treatment group

	Placebo (n = 24)	Vitamin A (n = 24)
Weight gain (Kg)	0.90 ± 0.14*	1.29 ± 0.17†
Diarrhea episodes	12	6
Score per episode of diarrhea	2.25 ± 0.25	2.17 ± 0.31
URTI episodes	9	7
Score per episode of URTI	2.66 ± 0.17	1.71 ± 0.28
Pneumonia episodes	6	5
Score per episode of pneumonia	6.67 ± 0.67	4.40 ± 0.98‡
CXR score ≥3	6	2
Score per CXR	3.83 ± 0.40	3.00 ± 0
IMS	5.74 ± 1.17	2.21 ± 0.45‡

* $\bar{x}$ ± SE.
†‡ Significantly different from placebo: †P = 0.04, ‡P = 0.02.

serious because of the synergistic effects of vitamin A deficiency and measles infection. Vitamin A–deficiency states have been shown to result in destruction of epithelial tissue and to depress the immune function (32). Measles virus produces similar effects (22).

The exact mechanism by which vitamin A reduces morbidity in measles patients is unknown. Two mechanisms that have been suggested are improvement of immune function and regeneration of damaged epithelial tissue (32). We studied some aspects of immune function [interleukin 2 & (IL-2), measles immunoglobulin G (IgG) antibody, total lymphocytes, and C_3] and found that vitamin A had an effect on the measles IgG antibody response and on total lymphocyte numbers (A Coutsoudis, P Kiepiela, HM Coovadia, M Broughton unpublished observations, 1991). It seems likely that the improvement in morbidity in the vitamin A–supplemented patients was due to nonspecific immune enhancement because of reestablishment of the integrity of the epithelial tissues of the respiratory and gastrointestinal tracts.

TABLE 5
Six-month morbidity outcome in children with measles, by treatment group

	Placebo (n = 16)	Vitamin A (n = 20)
Weight gain (kg)	2.37 ± 0.20*	2.89 ± 0.23
Diarrhea episodes	6	3
Score per episode of diarrhea	2.17 ± 0.31	1.67 ± 0.67
URTI episodes	8	3†
Score per episode of URTI	2.37 ± 0.18	2.00 ± 0.58
Pneumonia episodes	3	0†
Score per episodes of pneumonia	6.67 ± 0.67	0‡
CXR score ≥3	3	0†
Score per CXR	3.67 ± 0.67	0§
IMS	4.12 ± 1.13	0.60 ± 0.22

* $\bar{x}$ ± SE.
†‡§‖ Significantly different from placebo: †P = 0.05, ‡P = 0.005, §P = 0.01, ‖P = 0.002.

The results in this study on the beneficial effect of vitamin A during measles infection confirm the growing body of information linking vitamin A deficiency with increased susceptibility to infection (33) and the potential for reversing this by nutritional intervention. Perplexing evidence, however, has emerged in recent studies as to which sites of infection are more affected by vitamin A, eg, respiratory or enteric (34–37). Multiple studies to date suggest that vitamin A supplementation may improve the prognosis for respiratory infection more than for diarrhea. Our study supports this body of evidence, as we showed that vitamin A supplementation speeded up the recovery from pneumonia and reduced the number and severity of postmeasles respiratory infections but it had no significant effect on diarrhea. Our experience with measles over the last 20 y has shown that measles mortality is mainly due to pneumonia rather than to a direct relationship with diarrhea.

The lower-than-usual hospital-case fatality rate (12–14%) in this study could be accounted for by the absence of emergency cases and severe malnutrition.

Although follow-up was unsatisfactory, the strength of the study was increased by assessing patients at age 6 mo. The importance of follow-up of patients is underlined by two points: measles is followed by an excess of mortality for 12 mo after the rash appears (9, 18), and furthermore results from a vitamin A trial in the United States, in preterm neonates with bronchopulmonary dysplasia, revealed deaths at 6 mo after completion of the study (38).

The main strength of our study was that the morbidity data were carefully documented (with both clinical and radiological data for pneumonia) and the IMS for each child was determined immediately after the appointment, before the trial code was broken to eliminate any possible bias. Although only 60 children were involved, the power of the study was increased by concentrating on a very small age group (4–24 mo), which was the group shown to benefit most against mortality from vitamin A supplementation (12), to be most at risk for suffering ill effects with hyporetinemia (11), and to be affected most commonly by measles in Third-World countries (22).

Our results confirm the findings of a recent trial investigating the effects of vitamin A supplementation on measles mortality and morbidity (35), which showed that vitamin A supplementation resulted in a significant reduction in mortality and morbidity in the acute phase of measles in children from a community where clinical signs of vitamin A deficiency are uncommon.

The careful consideration of multiple covariants enhances the validity of the data obtained in this study and supports the current WHO recommendations for vitamin A supplementation during measles.

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References

1. Sommer A, Tarwotjo I, Hussaini G, Susamto D. Increased mortality in children with mild vitamin A deficiency. Lancet 1983;2:585–8.
2. Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory disease and diarrhoea in children with preexisting mild vitamin A deficiency. Am J Clin Nutr 1984;40:1090–5.
3. Milton RC, Reddy V, Naidu AN. Mild vitamin A deficiency and childhood morbidity—an Indian experience. Am J Clin Nutr 1987;46:827–9.
4. Sommer A, Tarwotjo I, Djunaedi E, et al. Impact of vitamin A supplementation on childhood mortality. A randomised controlled community trial. Lancet 1986;1:1169–73.
5. Rahmathullah L, Underwood B, Thulasiraj RD, et al. Reduced mortality among children in Southern India receiving a small weekly dose of vitamin A. N Engl J Med 1990;323:929–35.
6. Martorell R. Vitamin A deficiency and child health and survival. Food Nutr Bull 1989;11:3–4.
7. Forman MR. Research priorities and strategies for investigation of the influence of vitamin A supplementation on morbidity. Food Nutr Bull 1989;11:25–35.
8. Reddy V, Bhaskaram P, Raghuramulu N, et al. Relationship between measles, malnutrition, and blindness: a prospective study in Indian Children. Am J Clin Nutr 1986;44:924–30.
9. Bhaskaram P, Reddy V, Raj S, Bhatnagar RC. Effect of measles on the nutritional status of preschool children. J Trop Med Hyg 1984;87:21–5.
10. Varavithya W, Stoecker B, Chaiyaratana W, Kittikool J. Vitamin A status of Thai children with measles. Trop Geogr Med 1986;38:359–61.
11. Markowitz LE, Nzilambi N, Driskell WJ, et al. Vitamin A levels and mortality among hospitalized measles patients, Kinshasa, Zaire. J Trop Pediatr 1989;35:109–12.
12. Barclay AJG, Foster A, Sommer A. Vitamin A supplements and mortality related to measles: a randomised clinical trial. Br Med J 1987;294:294–6.
13. Ellison JB. Intensive vitamin therapy in measles. Br Med J 1932;2:708–11.
14. World Health Organization. Expanded programme on immunization: programme for the prevention of blindness nutrition. Joint WHO/UNICEF statement. Vitamin A for measles. Wkly Epidemiol Rec 1987;62:133–4.
15. Ferrinho P. National Workshop on measles immunization. S Afr Med J 1989;76:82–3.
16. Aaby P, Coovadia H, Bukh J, et al. Severe measles: a reappraisal of the role of nutrition, overcrowding and virus dose. Med Hypotheses 1985;18:93–112.
17. Coovadia HM, Wesley AW, Brain P, Hallett AF, Henderson LG, Vos G. Immunoparesis and outcome in measles. Lancet 1977;1:619–21.
18. Koster FT, Curlin GC, Aziz KMA, Haque A. Synergistic impact of measles and diarrhoea on nutrition and mortality in Bangladesh. Bull World Health Organ 1981;59:901–8.
19. Konno T, Hansen JDL, Truswell AS, Wood-Walker R, Becker D. Vitamin A deficiency and protein-calorie malnutrition in Cape Town. S Afr Med J 1968;42:950–5.
20. Kuming BS, Politzer WM. Xerophthalmia and protein malnutrition in Bantu children. Br J Ophthalmol 1976;51:649–66.
21. Argent AC, Rothberg AD, Kuyl J. Vitamin A and zinc status of mother-infant pairs at three South African hospitals. Pediatr Rev Commun 1989;3:343–50.
22. Coovadia, HM. Measles. Med Int 1988;51:2177–81.
23. Wesley AG, Coovadia HM, Kiepiela P. Further predictive indices of clinical severity of measles. S Afr Med J 1982;61:663–5.
24. Morley D. Paediatric priorities in the developing world. London: Butterworths, 1973.

25. Aaby P. Malnutrition and overcrowding/intensive exposure in severe measles infection: review of community studies. Rev Infect Dis 1988;10:478–91.
26. Solon FS, Popkin BM, Fernandez TL, Latham MC. Vitamin A deficiency in the Philippines: a study of xerophthalmia in Cebu. Am J Clin Nutr 1978;31:360–8.
27. Solomons NW, Russel RM. The interaction of vitamin A and zinc: implications for human nutrition. Am J Clin Nutr 1980;33:2031–40.
28. Jagadeesan V, Reddy V. Interrelationship between vitamins E and A: a clinical study. Clin Chim Acta 1978;90:71–4.
29. Rhys Williams, AT. Simultaneous determination of serum vitamin A and E by liquid chromatography with fluoresence detection. J Chromatogr 1985;341:198–201.
30. Interdepartmental Committee on Nutrition for National Defense. Manual for nutrition surveys. 2nd ed. Bethesda, MD: National Institutes of Health, 1963.
31. Coutsoudis A, Coovadia HM, Broughton M, Salisbury RT, Elson I. Micronutrient utilisation during measles treated with vitamin A or placebo. Int J Vitam Nutr Res (in press).
32. Barker BM. Vitamin A. In: Barker BM, Bender DA, eds. Vitamins in medicine. Vol 2. 4th ed. London: Heinemann, 1983:211–90.
33. Scrimshaw N, Taylor CE, Gordon JE. Interactions of nutrition and infection. WHO monograph series no. 57. Geneva: World Health Organization, 1968.
34. Bloem MW, Wedel M, Egger RJ, et al. Mild vitamin A deficiency and risk of respiratory tract diseases and diarrhea in preschool and school children in northeastern Thailand. Am J Epidemiol 1990;131:332–9.
35. Hussey GD, Klein M. A randomized, controlled trial of vitamin A in children with severe measles. N Engl J Med 1990;323:160–4.
36. West KP Jr, Howard GR, Sommer A. Vitamin A and infection: public health implications. Annu Rev Nutr 1989;9:63–86.
37. Pinnock CB, Douglas RM, Badcock NR. Vitamin A status in children who are prone to respiratory tract infections. Aust Paediatr J 1986;22:95–9.
38. Shenai JP, Kennedy KA, Chytil F, Stahlman MT. Clinical trial of vitamin A supplementation in infants susceptible to bronchopulmonary dysplasia. J Pediatr 1987;111:269–77.

11. Kenna MA, Bluestone CD, Fall P, Stephenson J, Kura-Lasky M, Wucher FP, et al. Cefixime *vs.* cefaclor in the treatment of acute otitis media in infants and children. Pediatr Infect Dis J 1987;6:992–6.
12. Mclinn SE. Randomized, open label, multicenter trial of cefixime compared with amoxicillin for treatment of acute otitis media with effusion. Pediatr Infect Dis J 1987;6:997–1001.
13. Cantor RM. The diagnosis and management of urinary tract infection in infants and children. Top Emerg Med 1990;12:58–64.
14. Feld LC, Greenfield SP, Ogra PL. Urinary tract infections in infants and children. Pediatr Rev 1989;11:71–7.
15. McCracken GH Jr. Options in antimicrobial management of urinary tract infections in infants and children. Pediatr Infect Dis J 1989;8:552–5.
16. Andriole VT. Urinary tract agents: quinolones, nitrofurantoin and methenamine. In Mandell GL, Douglas RG Jr, Bennetit JE, eds. Principles and practice of infectious diseases. 2nd ed. New York: Wiley, 1985:244–53.
17. Holmberg L, Boman G, Böttiger LE, et al. Adverse reactions to nitrofurantoin: an analysis of 921 reports. Am J Med 1980;69:733–8.
18. Ayd FJ. Once-a-day neuroleptic and tricyclic antidepressant therapy. Int Drug Ther Newslett 1972;7:33.
19. Ruff ME, Schotik DA, Bass JW, Vincent JM. Antimicrobial drug suspensions: a blind comparison of taste of fourteen common pediatric drugs. Pediatr Infect Dis J 1991;10:30–3.

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Vitamin A supplementation enhances specific IgG antibody levels and total lymphocyte numbers while improving morbidity in measles

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The effect of vitamin A supplementation on selected factors of immunity was tested in African children (ages 4 to 24 months with complicated measles) during a randomized double-blind intervention trial. Placebo (n = 31) and treated groups (n = 29) had similar baseline characteristics. The supplemented group had significant reductions in morbidity (expressed as integrated morbidity scores) during the acute (Day 8, P = 0.006) and chronic (Day 42, P = 0.02; 6 months; P = 0.002) phases. In the treated group there was an increase in total number of lymphocytes (Day 42, P = 0.05) and measles IgG antibody concentrations (Day 8, P = 0.02), both of which have consistently been previously shown to correlate more closely with outcome in measles than other immunologic, clinical and radiologic factors. Interleukin 2 and plasma complement values were unaffected by vitamin A supplementation. These findings reinforce results from animal studies that show that the pathways of vitamin A activity in decreasing morbidity and mortality are partly founded on selective immunopotentiation.

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INTRODUCTION

Recent evidence has shown that vitamin A deficiency, arising from inadequate diets or induced by infections,[1] is associated with increased morbidity[2, 3] and mortality.[4] Sickness and death in these circumstances are often a result of respiratory infections and occasionally of diarrheal diseases. Measles accentuates or precipitates decreased serum concentrations of vitamin A resulting in ocular damage and increased mortality rates. Field- and hospital-based studies have documented striking reductions in overall[5] and measles-specific[6, 7] morbidity and mortality after supplementation with vitamin A.

it is not clear how vitamin A deficiency predisposes to infection. The two most likely mechanisms appear to be damage to epithelial membranes and depression of immune responses. Animal studies have shown that vitamin A deficiency results in a wide range of impaired immune responses and that the effect is reversed by vitamin A supplementation.[8-10] Although much work has been done in animals there is limited information available from human studies, particularly in children who are most at risk for deficiency. Moreover much of the human data on vitamin A and immunity is confounded by the concomitant presence of protein energy malnutrition, itself a cause of severe immunodeficiency. The existing evidence suggests that the major detrimental effect of inadequate vitamin A is on nonspecific defense mechanisms, cell-mediated immunity and T-dependent B cell responses.[11, 12]

We explored some aspects of the immune reaction during a vitamin A supplementation study on measles morbidity in African children from a region where xerophthalmia is uncommon and is most often detected in association with protein energy malnutrition.[13, 14] We studied the effect of vitamin A supplementation on the production of measles IgG antibody and total lymphocyte numbers, interleukin 2 (IL-2) and plasma complement (C3) concentrations. These tests were chosen because they represent different components of the immune response and, more importantly, because (with the exception of IL-2) they correlate with clinical outcome in measles infection.[15, 16]

METHODS

Patient selection and assignment to treatment. These were 60 African children (4 to 24 months of age) of poor socioeconomic background presenting at Durban's King Edward VIII Hospital with measles complicated by pneumonia and diarrhea severe enough to warrant admission to the Fevers Hospital (Clairwood Hospital). The diagnosis of measles was made on clinical grounds. Dietary and socioeconomic information was obtained from the mother/guardian after entering the child on the trial. Patients were admitted to the trial on weekday mornings between April and October, 1989.

Children >24 months or with rash duration >5 days and those who had received vitamin A supplements in the month before admission were excluded from the trial. Any child with clinical signs of vitamin A deficiency was excluded; it was decided that such a child would immediately be given a dose of vitamin A. At completion of the study it was noted that no child had been excluded for this reason.

The patients were allocated to treatment or placebo groups according to a table of random numbers. The treatment and placebo dropper bottles were number-coded. All investigators and patients involved in the study were blinded as to study group assignment.

Both groups received standard therapy and monitoring for measles and its complications. The trial group received vitamin A (retinyl palmitate; Arovit Drops®, Roche) either 100 000 IU (under 12 months) or 200 000 IU (12 months and over). The control group received an equivalent volume of placebo syrup. Vitamin A or placebo was administered by the same person (AC) on admission and on Days 2 and 8. The above dosage of vitamin A which was given to the experimental group was that recommended by the World Health Organization (WHO).[17] In addition the children were given another dose of vitamin A or placebo at the Day 42 follow-up appointment.

Written informed consent was obtained from the parent or guardian before a child was admitted to the trial. The study protocol was approved by the University of Natal Medical Faculty Ethics and Research Committee.

Determinants of measles severity that were considered. Apart from vitamin A status many other factors have been suggested as determinants of severity of measles. We therefore recorded these other factors to ensure that when the code was broken the comparability of the two groups could be considered, namely lymphocyte counts less than 2×10^9/liter[16]; objective analysis of extent of pneumonia on chest radiograph (CXR)[16]; C3 concentrations[15]; protein energy malnutrition determined by weight/age centiles according to the National Center for Health Statistics,[18] clinical features and serum albumin values; extent of rash[19]; and degree of overcrowding at home.[20] A higher overcrowding index could also be associated with decreased vitamin A intake.[21]

Morbidity assessment. Patients were followed up daily in hospital and assessed for duration of fever; diarrhea (3 or more loose or watery stools a day); and pneumonia (presence of tachypnea with retractions, crackles or wheezes and other less common complications). Incidences of herpes stomatitis and laryngotracheobronchitis were also recorded. Complete clinical recovery was the stage at which fever, diarrhea, pneumonia and other complications were clinically resolved. Children were discharged on Day 8 if they had recovered completely. Children returned for follow-up appointments on Day 42 and at 6 months at which time they had a full clinical examination by the same pediatrician (MB) and a CXR was taken. The CXR was scored by a blinded scorer. The severity of the abnormalities in the lung fields was graded by awarding points for areas of patchy consolidation to a maximum of four, one point being given for each of the following: atelectasis; involvement of the peripheral lung fields, either by emphysema or consolidation; and effusion. Each child was given a score from 0 to 7

for their CXR at Days 1 and 42 and at 6 months. A score above 3 has previously successfully been used as an index for severe measles.[16] In the interim between discharge and the 2 follow-up appointments morbidity data were collected from the mother's records and recall and outpatient records. An integrated morbidity score (IMS) was calculated for each child based on the following rating system: 0 to 4 for diarrhea, upper respiratory tract infection, pneumonia and laryngotracheobronchitis where 0 is not present, 1 is reported by mother or guardian, 2 is documented mild condition, 3 is documented severe condition not requiring hospitalization and 4 is a condition requiring hospitalization (For pneumonia and laryngotracheobronchitis the rating system is weighted by a factor of 2 for the Day 42 and 6-month IMS.); 0 to 2 for herpes, where 0 is absent, 1 is localized, and 2 is disseminated; and 3 to 7 for CXR rating. Each child was assigned such an IMS on Days 1 and 8 and immediately after the Day 42 and 6-month appointment, before the code was broken.

Biochemical and immune factors. On admission to the trial (day 1) and on Days 8 and 42 a blood sample was taken by venipuncture before any vitamin A or placebo had been administered. Serum was separated within 5 hours, aliquoted and stored at −70°C until analyzed (between 1 and 10 months) for albumin, vitamin A, C3, IL-2 and measles IgG antibody. During all procedures blood samples were protected from sunlight to prevent photodestruction of vitamin A. All analyses were done in duplicate.

Vitamin A (as retinol) was measured by normal phase high pressure liquid chromatography using fluorescence detection. The method used was a modification of a previously reported method.[22] We used a Hewlett-Packard HP 1090® high pressure liquid chromatography instrument attached to a programmable fluorescence detector (HP 1046A®). The column used was a normal phase microbore column (Spherisorb S3W®; Phase Sep, United Kingdom).

Albumin was determined by laser nephelometry in the routine biochemistry laboratory attached to King Edward VIII Hospital. C3 values were determined by laser nephelometry on Days 1, 8 and 42. Total lymphocyte counts were determined in the routine King Edward VIII Hospital hematology laboratory on Days 1 and 42.

IL-2 concentrations were determined in serum using a commercial radioimmunoassay kit supplied by Amersham (Aylesbury, Buckinghamshire, United Kingdom; code RPA. 531). The kits were all supplied from the same batch (Batch 9B, Lot 85). A standard solution of human recombinant IL-2 (Met^0, Ala^{125}) in a concentration of 6.41 pmol/ml was supplied with the kit. For each run of 40 duplicate tests this standard was diluted serially to give 6 standard concentrations ranging from 2.5 to 320 fmol/ml and a standard curve was set up. The correlation coefficient between the 5 standard curves was 0.99 The 3 consecutive sera (days 1, 8 and 42) of each patient were tested in the same run and approximately equal numbers of patients from each group were tested on the same run. All results are reported as IU/ml. The standard used has been calibrated by Amersham against the IL-2 WHO First International Standard 86/504 and 1 IU was found to be equivalent to 5.3 fmol IL-2 (Met^0, Ala^{125}).

Measles IgG antibody was detected by means of the enzyme-linked immunosorbent assay (Behringwerke AG, Marburg, Germany). Measles antigen-coated plates were all supplied from the same batch (OSOK 02103 Lot 406446A) as were the anti-human IgG alkaline phosphatase conjugate (OSDH 04/05 Lot 410955A) and supplementary agents (Lot 19604). The 3 consecutive sera (Days 1, 8 and 42) of each patient were tested on the same plate. In addition approximately equal numbers of patients from each group were tested on the same plate in order to avoid any bias in sample testing. A series of 7 international and local standards as controls (2 of which were donated by Dr. Roger Glass, Centers for Disease Control, Atlanta, GA) were repeated 10 times and mean values were assigned to each of the 7 standards. For each run of 4 plates these same standards were set up and a regression analysis was performed. A correlation coefficient <0.987 resulted in the tests of that run being repeated. All the readings were corrected according to the standards. Results are expressed as mIU/ml with reference to the WHO standard anti-measles serum (obtained as a gift from WHO). The standard curve was obtained by using different concentrations of WHO measles reference serum plotted against optical density readings.

Controls. These consisted of 20 adequately nourished African children 4 to 24 months of age. Nutritional status was determined by anthropometric measurements and biochemical indicators (serum albumin, prealbumin, retinol-binding protein, zinc, vitamin A and E concentrations). These children were in the orthopedic and surgical wards for minor operations, e.g. hernia, or else they were from the well baby clinic in Kwa Mashu (Durban). All blood samples were taken before any surgical procedures. These controls were used to establish normal values for nutritional parameters, C3, absolute lymphocyte numbers and IL-2.

Statistical methods. All values are reported as mean ± SE. Differences in proportions in the data were examined by the chi square test. Differences in the means were examined by Student's two-tailed *t* test (Tables 1 to 3). The level of significance used was 5%. In addition because of intrasubject variability in immune factors mean of change from baseline for each group was determined at Days 8 and 42. Thus each child had a baseline determination on Day 1 from which a change in concentration at a specific time could be calculated. Individual changes were summed

and a mean value for change in concentration for each group was determined and expressed as a delta value. The two groups were compared with regard to these changes using the two sample *t* test with a Bonferroni adjustment; thus the significance level changed to alpha/2 (2.5%).

The software used for the computerized analysis of results was Statistical Analysis System (SAS)-Release 6.03 edition, 1988 (SAS Institute Inc, Cary, NC).

RESULTS

Baseline comparability. Baseline characteristics that are covariants of severe disease (age, nutritional status, socioeconomic status, morbidity at presentation and radiologic presentation) of the vitamin A (n = 29) and placebo (n = 31) groups were comparable (Table 1).

Morbidity outcome. A significantly higher number of vitamin A-supplemented children had recovered from complicated measles within 8 days compared with the placebo group (96% *vs.* 65%). The vitamin A group showed a marked reduction in morbidity for up to 6 months as indicated by significantly lower IMSs than the placebo group on Days 8 and 42 and at 6 months (Table 2). The reduction in morbidity was mainly caused by a decrease in incidence and severity of respiratory infections. Details of morbidity outcome are presented by Coutsoudis et al.[23]

Immune factors. On Day 1 there was no difference between the two groups in all the immune factors tested (Table 3).

On Day 1 lymphocyte numbers were decreased in placebo- and vitamin A-treated groups compared with controls (P = 0.005); however, they increased within both groups during the next 6 weeks to return to normal values by Day 42. On Day 42 the vitamin A-treated group had higher lymphocyte numbers than the placebo group, P = 0.05 (Table 3). When analyzing the changes in lymphocyte numbers (day 42–day 1) we found the same trend that the rate of change was greater in the treated group (delta = 3.40 ± 0.74 *vs.* 1.96 ± 0.51, P = 0.06); however, this was not statistically significant.

The mean concentrations of measles IgG antibody were significantly increased within both groups during the first 6 weeks. On Days 8 and 42 the vitamin A-treated groups had higher mean antibody values. This difference was significant on day 8, P = 0.01 (Table 3; Fig. 1). On analysis of the changes in antibody concentrations a similar trend was found with the changes between Day 8 and Day 1 being significantly higher in the treated group (delta = 340.6 ± 49.6 *vs.* 182.3 ± 27.6, P = 0.008). The changes between Day 42 and Day 1 were also higher in the treated group (delta = 820.7 ± 85.5 *vs.* 617.7 ± 88.5) although this difference did not reach statistical significance.

On Day 1 C3 values in both groups were depressed compared with controls (P = 0.003) but by Day 42 they had attained control values. IL-2 concentrations on admission were also depressed compared with controls (P = 0.02) but by Day 8 they had reached normal control values. C3 and IL-2 values were not significantly different between the treated and placebo groups on Days 1, 8 and 42 (Table 3).

TABLE 1. Baseline characteristics of children with measles according to Treatment Group*

Characteristic	Placebo (n = 31)	Vitamin A (n = 29)
Age (months)	10.42 ± 0.70	12.17 ± 1.00
Males (no.)	13	16
Weight/age < 80 Std.† (no.)	9	9
Hemoglobin (g/dl)	11.05 ± 0.35	10.66 ± 0.31
Albumin (g/liter)	31.84 ± 0.65	30.10 ± 1.05
Vitamin A (μg/dl)	11.73 ± 1.05	12.22 ± 1.05
CXR score > 3 (no.)	5	7
Lymphocytes < 2 × 10⁶/liter (no.)	6	4
Lymphocytes < 2 × 10⁶/liter and CXR score > 3 (no.)	1	2
C3 (g/liter)	1.02 ± 0.03	1.14 ± 0.06
Overcrowding index‡	2.68 ± 0.44	2.65 ± 0.35
Rash grade§	2.13 ± 0.12	2.00 ± 0.12
IMS‖	9.82 ± 1.80	10.56 ± 1.96

* There is no significant difference between the groups for any of the characteristics, where applicable results presented as mean ± SE.
† 50th NCHS percentile; No child had clinical features of protein energy malnutrition.
‡ Number of persons/room.
§ 1, face; 2, face, trunk; 3, face, trunk, limbs.
‖ See "Morbidity assessment" for explanation.
NCHS, National Center for Health Statistics.

TABLE 2. Morbidity outcome of measles patients according to treatment group

Factor	n	Placebo	n	Vitamin A	P
Clinical recovery < 8 days (no.)	31	20	29	28	0.002
Day 8 IMS	30	1.37 ± 0.40*	29	0.24 ± 0.15	0.006
Day 42 IMS	24	5.74 ± 1.17	24	2.21 ± 0.45	0.02
6-month IMS	16	4.12 ± 1.13	20	0.60 ± 0.22	0.002
Day 42 weight gain (kg)	24	0.90 ± 0.14	24	1.29 ± 0.17	0.04
6-month weight gain (kg)	16	2.37 ± 0.20	20	2.89 ± 0.23	0.08

* Mean ± SE.

TABLE 3. Immune factors studied sequentially in placebo- and vitamin A-treated groups of children with measles (mean ± SE)

	Controls	Placebo			Vitamin A		
Day		1	8	42	1	8	42
n	20	31	30	20	29	28	21
Lymphocytes × 10^9/liter	5.72 ± 0.61*	3.80 ± 0.42		6.45 ± 0.66†	3.75 ± 0.41		8.10 ± 0.80†
C3 (g/liter)	1.32 ± 0.07‡	1.02 ± 0.03	1.11 ± 0.04	1.41 ± 0.11	1.14 ± 0.06	1.25 ± 0.07	1.48 ± 0.08
IL-2 (IU)/ml	1.79 ± 0.06§	1.57 ± 0.08	1.72 ± 0.08	1.70 ± 0.08	1.59 ± 0.06	1.76 ± 0.08	1.74 ± 0.08
IgG (mIU)/ml		39.9 ± 5.5	222.8 ± 28.7‖	654.8 ± 91.2	42.6 ± 5.3	384.2 ± 52.8‖	869.5 ± 90.0

*, ‡, § Control values significantly higher than Day 1 values of measles patients: *$P = 0.005$; ‡$P = 0.003$, §, $P = 0.02$.
† Difference between means on Day 42, $P = 0.05$.
‖ Significant difference between means on Day 8, $P = 0.01$.

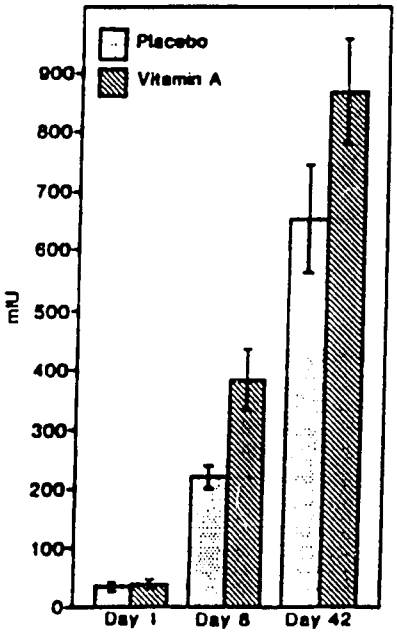

FIG. 1. Serum measles IgG antibody levels in placeo- and vitamin A-treated groups (mean ± SE).

DISCUSSION

This study has shown that a substantial and sustained reduction in morbidity in vitamin A-supplemented African children with measles was paralleled by elements of a more effective immune response. The latter was reflected in higher titers of specific IgG antibodies and a speedier reversal of the lymphopenia induced by virus infection.

These two factors are simple measurable indices of a considerably more elaborate network of immune reactions which prevent the initial infection, limit its spread once it has been established and finally eliminate the organism. However, there is clear evidence that specific antibody is of critical importance in measles: it persists for many years and correlates with protection; it is the single most widely utilized index of effective vaccination; maternal antibody provides fairly solid immunity to infants and often renders conventional vaccines ineffective; and gamma-globulin given during the incubation period aborts measles.[24] Alterations in peripheral blood lymphocyte numbers occur regularly in measles and are caused by changes in different subpopulations. The action of these subpopulations, which include HLA restricted cytotoxic T cells, K cells, natural killer cells and other less clearly defined groups, are believed to be responsible for containing the spread of infection and eliminating the virus. Lymphopenia is not uncommon in severe cases and we have shown previously that this decrease in circulating lymphocytes is mainly in the T helper cells.[25]

Despite the complexities of the immune response, we have found that in the clinical case of measles, depressed antibody values and lymphopenia are of considerable practical value in predicting outcome; 77% of children who had lymphopenia at onset of rash died or developed protracted pneumonia, and all who died failed to produce adequate measles antibodies.[26] In addition lymphopenia has been found to correlate strongly with clinical outcome in other infectious diseases besides measles.[27]

It has been known for some time that children with secondary immunodeficiency who fail to produce antibody develop fatal measles giant cell pneumonia.[28] As against this C3 values in measles are much less helpful in making a prognosis of severity.[16] Accordingly it is particularly significant that therapy with vitamin A produced an effect on these very components, i.e. antibodies and peripheral blood lymphocytes.

Measles impairs specific and nonspecific immune responses. Accordingly morbidity and mortality result from unrestricted measles and also from superinfection with opportunistic invaders. Therefore vitamin A supplementation through the augmented immune responses detected here may minimize the harmful effects of measles virus and also of other pathogens. This interpretation would be supported by our findings of the beneficial effect of vitamin A up to 6 months after the rash.

We suggest that the improvements in morbidity and the changes detected in antibody response and lymphocyte numbers are most likely caused by vitamin A supplementation because there were no significant differences between the two groups in all the variables considered.

We have not previously used IL-2 estimations as a predictive index in measles. However, given the central role played by cell-mediated immunity (including

cytotoxic T cells and T helper cells and their product IL-2) in controlling measles virus dissemination and killing in the body, we would have expected IL-2 concentrations to accompany improvements in morbidity produced by vitamin A. It is possible that our blood sampling was undertaken at too late a stage (Day 8) to detect rapid changes which could possibly have occurred earlier.[29] Quantitative values for IL-2 have not been adequately assessed in measles; we have shown here that IL-2 concentrations in patients were significantly reduced compared with those in healthy controls. This is consistent with our previous observation that T helper cells are depleted during measles. IL-2 is important in the clonal expansion of T helper cells and could therefore play a role in the observed low T helper cell numbers in measles.

With regard to the value of vitamin A intervention in reducing child population morbidity and mortality in regions where xerophthalmia is common, it is pertinent to point out that the beneficial effects on morbidity and aspects of the immune response shown here were produced in an infectious disease which is powerfully immunosuppressive and a major cause of sickness and death in the Third World. It is reasonable to expect more pronounced effects of vitamin A supplementation on immunity associated with improvements in morbidity for the common and less damaging respiratory tract infections and diarrheal diseases of infancy and childhood in developing countries.

The results reported here are consistent with animal studies on the effects of vitamin A on immune function.[8-10] However, one clinical trial among Bangladeshi children failed to show any effect of vitamin A supplementation on anti-tetanus toxoid antibody titers.[30]

The exact pathway by which vitamin A might improve aspects of the immune response noted in this study is unclear; likely mechanisms are more effective specific immunity caused by improved T helper cell-mediated antibody synthesis[11] and adjuvanticity.[31]

This study confirms and extends previous observations that have shown that the immunoparesis secondary to measles is transient and that normal values for most tests of immune function are attained by about 6 weeks after the exanthematous phase of the disease.[32]

We conclude that vitamin A supplementation had an effect on immune function as shown by speedier reversal of measles induced lymphopenia and by improvement of the measles IgG antibody response during the acute phase. The effect of supplementation on measles antibody is relevant to the WHO Expanded Programme for Immunization, which recommends that children in vitamin A-deficient communities should be given vitamin A at the time of immunization. A heightened antibody response could lead to a reduction in the number of vaccine failures that occur in developing countries.

Because vitamin A appears to play such an important role in reducing morbidity and mortality we suggest that more extensive and subtle tests of immune function be studied. More investigations are also necessary to establish the role of vitamin A in restoring and maintaining epithelial integrity with resulting improvements of nonspecific immunity.

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REFERENCES

1. Inua M, Duggan MB, West CE, Whittle HC, Kogbe OI, Sandford-Smith JH, et al. Post-measles corneal ulceration in children in northern Nigeria: the role of vitamin A, malnutrition and measles. Ann Trop Pediatr 1983;3:181-91.
2. Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory disease and diarrhoea in children with preexisting mild vitamin A deficiency. Am J Clin Nutr 1984;40:1090-5.
3. Milton RC, Reddy V, Naidu AN. Mild vitamin A deficiency and childhood morbidity: an Indian experience. Am J Clin Nutr 1987;4:827-9.
4. Sommer A, Tarwotjo I, Hussaini G, Susanto D. Increased mortality in children with mild vitamin deficiency. Lancet 1983; 2:585-8.
5. Sommer A, Tarwotjo I, Djunaedi E, West KP Jr, Loeden AA, Tilden R, et al. Impact of vitamin A supplementation on childhood mortality: a randomised controlled community trial. Lancet 1986;1:1169-73.
6. Barclay JG, Foster A, Sommer A. Vitamin A supplements and mortality related to measles: a randomised clinical trial. Br Med J 1987;294:294-6.
7. Hussey GD, Klein M. A randomized, controlled trial of vitamin A in children with severe measles. N Engl J Med 1990;323: 160-4.
8. Cohen BE, Elin RJ. Vitamin A-induced nonspecific resistance to infection. J Infect Dis 1974;129:597-600.
9. Naus KM, Mark DA, Suskind RM. The effect of vitamin A deficiency on the *in vitro* cellular immune response of rats. J Nutr 1979;109:1815-23.
10. Jurin M, Tannock IF. Influence of vitamin A on immunological response. Immunology 1972;23:283-7.
11. West KP Jr, Howard GR, Sommer A. Vitamin A and infection: Public health implications. Annu Rev Nutr 1989;9:63-86.
12. Chandra RK, Vyas D. Vitamin A, immunocompetence and infection. Food Nutr Bull 1989;11:12-9.
13. Konno T, Hansen JDL, Truswell AS, Wood-Walker R, Becker D. Vitamin A deficiency and protein-calorie malnutrition in Cape Town. S Afr Med J 1968;42:950-5.
14. Kuming BS, Politzer WM. Xerophthalmia and protein malnutrition in Bantu children. Br J Ophthalmol 1976;51:649-66.
15. Coovadia HM, Wesley AW, Brain P, Hallett AF, Henderson LG, Vos G. Immunoparesis and outcome in measles. Lancet 1977;1:619.
16. Wesley AG, Coovadia HM, Kiepiela P. Further predictive indices of clinical severity of measles. S Afr Med J 1982;61: 663-5.
17. Expanded Programme on Immunization. Programme for the prevention of blindness nutrition. Joint WHO/UNICEF statement Vitamin A for measles. Wkly Epidemiol Rec 1987;62: 133-4.

18. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roach AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. Am J Clin Nutr 1979;32:607–29.
19. Morley D. Paediatric priorities in the developing world. London: Butterworths, 1973:207–30.
20. Aaby P. Malnutrition and overcrowding/intensive exposure in severe measles infection: review of community studies. Rev Infect Dis 1988;10:478–91.
21. Solon FS, Popkin BM, Fernandez TL, Latham MC. Vitamin A deficiency in the Philippines: a study of xerophthalmia in Cebu. Am J Clin Nutr 1978;31:360–8.
22. Rhys Williams AT. Simultaneous determination of serum vitamin A and E by liquid chromatography with fluorescence detection. J Chromatogr 1985;341:198–201.
23. Coutsoudis A, Broughton M, Coovadia HM. Vitamin A supplementation reduces measles morbidity in young African children: a randomized placebo controlled double blind trial. Am J Clin Nutr 1991;54:890–5.
24. Coovadia HM. Host allergic response variation in children with measles infection (MD thesis). Durban, South Africa: University of Natal, 1977;94pp.
25. Kiepiela P, Coovadia HM, Coward P. T Helper cell defect related to severity in measles. Scand J Infect Dis 1987;19: 185–92.
26. Coovadia HM, Wesley A, Brain P. Immunological events in acute measles influencing outcome. Arch Dis Child 1978;53: 81–7.
27. Barnes PF, Leedom JM, Chan LS, Wong SF, Shah J, Vachon LA, et al. Predictors of short-term prognosis in patients with pulmonary tuberculosis. J Infect Dis 1988;158:366–71.
28. Coovadia HM. Measles. Med Int 1988;51:2177–81.
29. Griffin DE, Moench TR, Johnson RT, De Soriano IL, Vaisberg A. Peripheral blood mononuclear cells during measles infection: cell surface phenotypes and evidence for activation. Clin Immunol Immunopathol 1986;40:305–12.
30. Brown KH, Rayan MM, Chakraborty J, Aziz KM. Failure of a large dose of vitamin A to enhance the antibody response to tetanus toxoid in children. Am J Clin Nutr 1980;33:212–7.
31. Dresser DW. Adjuvanticity of Vitamin A. Nature 1968;217: 527–9.
32. Wesley A, Coovadia HM, Henderson L. Immunological recovery after measles. Clin Exp Immunol 1978;32:540–4.

A RANDOMIZED, CONTROLLED TRIAL OF VITAMIN A IN CHILDREN WITH SEVERE MEASLES

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Abstract *Background.* Measles kills about 2 million children annually, and there is no specific therapy for the disease. It has been suggested that vitamin A may be of benefit in the treatment of measles.

Methods. We conducted a randomized, double-blind trial involving 189 children who were hospitalized at a regional center in South Africa because of measles complicated by pneumonia, diarrhea, or croup. The children (median age, 10 months) were assigned to receive either vitamin A (total dose, 400,000 IU of retinyl palmitate, given orally; n = 92) or placebo (n = 97), beginning within five days of the onset of the rash. At base line, the characteristics of the two groups were similar.

Results. Although clinically apparent vitamin A deficiency is rare in this population, the children's serum retinol levels were markedly depressed (mean [±SEM], 0.405±0.021 μmol per liter [11.6±0.6 μg per deciliter]), and 92 percent of them nad hyporetinemia (serum retinol level <0.7 μmol per liter [20 μg per deciliter]). Serum concentrations of retinol-binding protein (mean, 30.1±2.0 mg per liter) and albumin (mean, 33.4±0.5 g per liter) were also low. As compared with the placebo group, the children who received vitamin A recovered more rapidly from pneumonia (mean, 6.3 vs. 12.4 days, respectively; P<0.001) and diarrhea (mean, 5.6 vs. 8.5 days; P<0.001), had less croup (13 vs. 27 cases; P = 0.03), and spent fewer days in the hospital (mean, 10.6 vs. 14.8 days; P = 0.01). Of the 12 children who died, 10 were among those given placebo (P = 0.05). For the group treated with vitamin A, the risk of death or a major complication during the hospital stay was half that of the control group (relative risk, 0.51; 95 percent confidence interval, 0.35 to 0.74).

Conclusions. Treatment with vitamin A reduces morbidity and mortality in measles, and all children with severe measles should be given vitamin A supplements, whether or not they are thought to have a nutritional deficiency. (N Engl J Med 1990; 323:160-4.)

MEASLES remains a devastating disease, for which specific therapy is lacking. Hopes for its control and eventual eradication rest on immunization, but measles kills about 2 million children each year[1] and cripples an untold number through blindness[2] and lung disease.[3,4] The idea that vitamin A may have a protective effect in measles was first suggested more than 50 years ago[5] but was ignored until Barclay et al.,[6] in a randomized clinical trial, found twice as many deaths in the control group (12 of 92) as among children given high doses of vitamin A (6 of 88).[6] Although the overall results did not reach statistical significance, vitamin A was significantly protective in the group under two years of age.[6]

That vitamin A should be of benefit in measles is biologically plausible.[7] Measles depresses serum levels of vitamin A,[8-11] and hyporetinemia (a serum retinol level below 0.7 μmol per liter [20 μg per deciliter]) is associated with increased mortality from the disease, particularly in children under two years of age.[11] In almost every known infectious disease, vitamin A deficiency is known to result in greater frequency, severity, or mortality.[12] Increased susceptibility to infection was one of the first features of nutritional vitamin A deficiency to be recognized,[13] and even mild deficiency appears to be associated with an increased risk of pneumonia, diarrhea, and death in childhood.[14-17] According to Scrimshaw et al., "no nutritional deficiency in the animal kingdom is more consistently synergistic with infection than that of vitamin A."[12] They list nearly 50 studies (including 8 in humans) of diseases of bacterial, viral, or protozoan origin in which vitamin A deficiency resulted in increased frequency, severity, or mortality.[12] In fact, vitamin A is sometimes referred to as the "anti-infective" vitamin.[18]

We embarked on this study because measles is a pressing problem in our part of the world[19] and because the results of Barclay et al.[6] and the circumstantial evidence appeared promising. Subsequently, acting on the same evidence, the World Health Organization recommended routine vitamin A supplementation for all children with measles in regions where vitamin A deficiency was a recognized problem and suggested that elsewhere "in countries where the fatality rate of measles is 1% or higher it would be sensible to provide vitamin A supplements to all children diagnosed with measles."[20] One difficulty with this advice is that in the communities in which measles poses the greatest problem, the mortality rate is often unknown. Another is that the recommendation is based on the less than conclusive evidence from the only two studies to have addressed the question of vitamin A therapy in measles.[5,6] These are some of the reasons why vitamin A supplementation is still not given routinely to children who are seriously ill with measles in South Africa, and presumably elsewhere.

METHODS

Children with acute measles who required hospital admission for the treatment of associated complications were entered in a randomized, double-blind, placebo-controlled trial to assess the effect of oral vitamin A on morbidity and mortality. The study was limited by a priori considerations to a fixed termination date, with a maximal enrollment of 200 cases. It was conducted from March to July 1987 at the City Hospital for Infectious Diseases, a regional center serving a population of about 2 million in Cape Town and

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surrounding areas. The Medical Faculty's ethics and research committee approved the study protocol.

Patient Selection and Randomization

All children under 13 years of age who were referred to the hospital for admission with measles were eligible for entry into the trial. The criteria for exclusion were vitamin A therapy before admission, xerophthalmia on admission or thereafter, rash for more than four days, or lack of parental consent.

Patients in the trial were randomly assigned to receive either 400,000 IU (120 mg) of water-miscible vitamin A (retinyl palmitate; Arovit drops, Roche, Basel, Switzerland) or an identical-appearing placebo from syringes coded according to a random-number table. The senior ward nurse gave half the dose on admission and the remainder a day later, either by mouth or by nasogastric tube. The children were cared for by the regular ward staff. Concurrent therapy included oxygen, intravenous fluids, and antibiotics as appropriate, but no additional vitamin supplements. One of the study investigators assessed the patients each day. The treatment-assignment codes were broken only at the completion of the trial.

Initial Investigations

The children's weight and height were recorded, and a venous-blood sample was drawn on entry into the trial. The weights and heights were evaluated against the standards of the National Center for Health Statistics.[21] Hemoglobin levels, white-cell counts (by Coulter model S5, Coulter Electronics, Hialeah, Fla.), and differential counts were estimated, and serum was stored at −70°C. Serum levels of total protein and albumin were measured by automated analysis (Astra-8, Beckman Instruments, Brea, Calif.). Serum concentrations of vitamin A (as retinol) were measured by high-performance liquid chromatography (Dupont Instruments, Wilmington, Del.), with concentrations of vitamin E (as alpha-tocopherol) obtained incidentally.[22] A programmable integrator was used to quantify the chromatographic results (Spectra-Physics, San Jose, Calif.). Retinol-binding protein was measured by radial immunodiffusion with a commercial kit (LC-Partigen, Behringwerke, Marburg, Federal Republic of Germany). Chest radiography and other investigations were performed when indicated.

Table 1. Base-Line Clinical Findings in 189 Children with Measles, According to Treatment Group.*

Characteristic	No. of Patients	Placebo (N = 97)	Vitamin A (N = 92)
Age (mo)		*15.06 (8, 10, 15)*	*15.89 (8, 10, 17)*
<6	7	3	4
6–12	117	64	53
13–23	37	18	19
≥24	28	12	16
Male/female		56/41	53/39
Mixed race/black		29/68	24/68
Weight for age†	189	*81.5 (74, 84, 92)*	*85.7 (77, 85, 96)*
<5th percentile	95	51	44
Height for age†	178	*96.0 (93, 97, 100)*	*97.1 (93, 96, 101)*
<5th percentile	52	25	27
Weight for height†	178	*89.0 (82, 88, 95)*	*90.3 (84, 91, 97)*
<5th percentile	70	41	29
Rash (days)‡		*1.91 (1, 2, 2)*	*1.72 (1, 1.5, 2)*
Diarrhea	152	75	77
No pneumonia	30	13	17
Pneumonia	146	74	72
No diarrhea	24	12	12
Pneumonia and diarrhea	122	62	60
Herpes stomatitis	4	1	3
Measles croup§	13	4	9

*Values in italics are means, followed in parentheses by 25th percentiles, medians, and 75th percentiles. All other values are numbers of patients.

†Expressed as a percentage of the 50th percentile of the standards of the National Center for Health Statistics.

‡P<0.05 for the comparison between groups.

§No patients with measles croup required airway interventions.

Assessment of Outcomes

Outcomes were assessed solely on the basis of clinical criteria. The outcome variables used were death and the severity of illness, as indicated by the duration of the hospital stay; the duration of pneumonia or diarrhea; the incidence of "postmeasles" croup or herpes stomatitis; and the need for a transfer to the Red Cross War Memorial Children's Hospital for intensive care. Pneumonia was defined as the presence of tachypnea (frequency of respiration >40 per minute) with retractions, crackles, or wheezes. Diarrhea was defined as the passage of four or more liquid stools a day. Measles croup was defined as croup presenting on or within a day of admission. Croup that developed subsequently was categorized as postmeasles.

Statistical Analysis

The data were analyzed by computer with the Epi-Info program (version 3, USD, Stone Mountain, Ga.). Categorical data[23] (e.g., the number of patients per group) were evaluated by the chi-square test, with Yates' correction for continuity applied routinely,[24] or by Fisher's exact test when the expected number in a cell was five or less.[24] Confidence intervals for the relative risks were calculated according to the method of Greenland and Robins.[25] Continuous data[23] (e.g., vitamin level) were compared by the nonparametric Kruskal–Wallis test.[24,26] All P values reported are two-tailed, with values of less than 0.05 considered statistically significant.

Results

Exclusion of Patients

Of 224 patients under 13 years of age who were admitted to the hospital with measles during the study, 35 were excluded from the trial. In 12 of these cases the rash was present for five or more days, in 2 vitamin A had previously been given, in 18 consent could not be obtained because the child was unaccompanied by a parent on admission, and in 3 the parents refused consent. Hence, 189 patients were entered in the trial. There were no exclusions for xerophthalmia or withdrawals after entry.

Base-Line Characteristics

The placebo and treatment groups were generally comparable (Tables 1 and 2), except that the patients in the vitamin A group were admitted about 12 hours earlier in terms of the duration of the rash and had lower serum levels of total protein and albumin than those in the placebo group. Two thirds of the children were 12 months old or younger (median, 10 months; range, 2 months to 5 years), and most were boys (58 percent). Blacks predominated (72 percent), and the remainder were of mixed race. The five white patients admitted with measles were excluded: consent was refused in the cases of two, and three were more than 13 years old. The hospital is open to all. Immunization and socioeconomic factors are thought to account for differences in racial makeup between the study population and the general population 14 years of age or

under in Cape Town (57 percent mixed race, 25 percent black, 18 percent white).[27] Heights were not measured for 11 patients. Height for age was below the fifth percentile in 52 children (29 percent) — a prevalence similar to that in the local reference population.[28] Weight for age (below the fifth percentile in 50 percent), and weight for height (below the fifth percentile in 39 percent) were considered to reflect short-term weight losses from measles[29,30] rather than preexisting acute protein-energy malnutrition, since that occurs in 1 percent or less of the local reference population.[28] A combination of pneumonia and diarrhea was the usual indication for hospital admission (64 percent). Diarrhea (16 percent), pneumonia (13 percent), or measles croup (7 percent) appearing as isolated symptoms precipitated the other admissions.

Table 2. Base-Line Blood and Serum Values, According to Treatment Group.

Characteristic*	No. of Patients	Placebo	Vitamin A
		mean (25th, 50th, and 75th percentile)	
Hemoglobin (g/dl)	177	10.73 (10, 10.6, 11.5)	10.78 (10, 10.5, 11.7)
Hematocrit (%)	177	32.4 (30, 32.5, 35)	32.8 (30, 32, 35)
Leukocytes ($\times 10^{-9}$/liter)	177	8.63 (6.3, 7.7, 10.2)	8.99 (6.2, 8.15, 10.25)
Lymphocytes ($\times 10^{-9}$/liter)	177	3.39 (2, 3.1, 4.2)	3.42 (1.8, 2.9, 4.3)
Total protein (g/liter)†	155	58.54 (55, 57, 62)	53.94 (51, 54, 58)
Albumin (g/liter)†		34.5 (32, 34, 37)	32.4 (29, 33, 35)
RBP (mg/liter)	156	29.6 (14, 18, 30)	30.48 (14, 17, 37)
Vitamin A (retinol) (μg/dl)	156	12.19 (7.7, 10.7, 14.4)	10.95 (6.7, 9.5, 12.6)
Age <2 yr	131	12.84 (11.4, 15.1, 46.5)	11.1 (6.7, 9.5, 12.4)
Age ≥2 yr‡	25	8.38 (7.1, 8.1, 10.5)	10.29 (6.4, 10.5, 13.6)
Hyporetinemia	143	68§	75§
Vitamin E (mg/liter)	156	7.94 (5.5, 7.9, 9.4)	6.84 (4.7, 6.8, 8.8)

*Reference values for the characteristics shown are as follows:[26] hemoglobin, 11.5 to 15.5 g per deciliter; hematocrit, 35 to 45 percent; leukocytes, 6 to 17×10^{9} cells per liter; total protein, 62 to 80 g per liter; albumin, 35 to 50 g per liter; retinol-binding protein, 22 to 45 mg per liter; vitamin A (as retinol), 30 to 80 μg per deciliter; vitamin E (as alpha-tocopherol), 5.0 to 20 mg per liter. No reference values are given for lymphocytes because of considerable variation with age. RBP denotes retinol-binding protein. To convert grams of hemoglobin per deciliter to millimoles per liter, multiply by 0.6206; to convert micrograms of vitamin A per deciliter to micromoles per liter, multiply by 0.03491; and to convert milligrams of vitamin E per liter to micromoles per liter, multiply by 23.22.

†$P<0.05$ for the comparison between groups.

‡In the placebo group, the retinol level was significantly lower in children ≥2 years old than in those <2 years old ($P = 0.026$).

§Indicates the number of cases of hyporetinemia (serum retinol concentration <0.7 μmol per liter [20 μg per deciliter]).

No blood samples were obtained from 15 patients, and only partial results were available for another 19 (Table 2). Serum levels were low for total protein (mean [±SE], 56.2±0.7 g per liter), albumin (mean, 33.4±0.46 g per liter), retinol-binding protein (mean, 30.1±2.02 mg per liter), and vitamin A as retinol (mean, 0.405±0.021 μmol per liter [11.6±0.6 μg per deciliter]). Low levels of total protein principally reflect depressed serum albumin concentrations ($r^2 = 72.6$ percent, $P<0.001$). Serum retinol levels were below the lower limit of the normal range (0.7 μmol per liter [20 μg per deciliter]) in 92 percent of the children (143 of 156), and 46 percent (72) had levels below 0.35 μmol per liter (10 μg per deciliter), placing them at risk for xerophthalmia,[31] although no cases of this were observed. Vitamin E levels were in the normal range.

Outcome

The children who received vitamin A had markedly diminished mortality and morbidity (Table 3), with no clinically apparent adverse effects. Of the 12 children who died (6.3 percent), 10 were in the placebo group ($P = 0.046$). The children who died were 5 to 29 months of age, and seven were boys. Death occurred 3 to 32 days after admission (median, 10.5). Pneumonia[32,33] caused 10 deaths, and the two remaining children died after 15 and 32 days, respectively, of fulminant sepsis following chronic diarrhea and measles-induced kwashiorkor. Croup was present as an incidental finding in 5 of the 10 children who died of pneumonia.

Cases of pneumonia lasted almost twice as long in the placebo group as in the vitamin A group ($P<0.001$), and 66 percent of the children with chronic pneumonia (>10 days) were in the placebo group ($P = 0.008$). Similarly, diarrhea continued for a third longer in the placebo group ($P<0.001$), and 72 percent of the children with chronic diarrhea were in that group ($P = 0.023$). Postmeasles croup was more common in the placebo group ($P = 0.033$), as was herpes stomatitis ($P = 0.08$). Finally, the hospital stay of the survivors was shorter by a third in the vitamin A–treated group ($P = 0.004$).

Overall, 77 children had adverse outcomes (Table 3), of whom 52 were in the placebo group ($P = 0.004$). As compared with the children in the placebo group, the children treated with vitamin A were at lower relative risk for death (relative risk, 0.21; 95 percent confidence interval, 0.05 to 0.94), prolonged pneumonia ≥10 days (relative risk, 0.44; 95 percent confidence interval, 0.24 to 0.80), prolonged diarrhea ≥10 days (relative risk, 0.40; 95 percent confidence interval, 0.19 to 0.86), postmeasles croup (relative risk, 0.51; 95 percent confidence interval, 0.28 to 0.92), airway intervention (relative risk, 0.35; 95 percent confidence interval, 0.10 to 1.26), herpes stomatitis (relative risk, 0.23; 95 percent confidence interval, 0.05 to 1.06), and the need for intensive care (relative risk, 0.38; 95 percent confidence interval, 0.13 to 1.16). The overall risk for an adverse outcome in children treated with vitamin A was half that in the control group (relative risk, 0.51; 95 percent confidence interval, 0.35 to 0.74). Of the 77 children who had adverse outcomes, only 2 were ≥2 years of age ($P = 0.002$), and the risk in a child ≥2 years old was substantially lower than in

Table 3. Mortality and Morbidity in 189 Children with Measles, According to Treatment Group.*

Characteristic	Placebo (N = 97)	Vitamin A (N = 92)	Relative Risk (95% CI)†	P Value
Death	10	2	0.21 (0.05–0.94)	0.046
Age at death (mo)				
<6	1	0		
6–12	7	1		
13–23	1	1		
≥24	1	0		
Pneumonia (days)				
Duration	*12.37 (5, 8, 17)*	*6.53 (3, 5, 8.5)*		<0.001
≥10	29	12	0.44 (0.24–0.80)	0.008
Diarrhea (days)				
Duration	*8.45 (5, 7, 10)*	*5.61 (3, 5, 7)*		<0.001
≥10	21	8	0.40 (0.19–0.86)	0.023
Postmeasles croup	27	13	0.51 (0.28–0.92)	0.033
With airway intervention	9	3	0.35 (0.10–1.26)	0.16
Herpes stomatitis	9	2	0.23 (0.05–1.06)	0.08
Intensive care	11	4	0.38 (0.13–1.16)	0.13
Adverse outcome‡	52	25	0.51 (0.35–0.74)	<0.001
Hospital stay (days)§	*15.24 (8, 11, 19)*	*10.52 (7, 9, 13)*		0.004

*In the columns representing the treatment groups, the values in italics are means, followed in parentheses by 25th percentiles, medians, and 75th percentiles. All other values are numbers of patients.

†Relative risk denotes the ratio of the incidence of an event in the vitamin A group to the incidence of the event in the placebo group. CI denotes confidence interval.

‡Defined as death, pneumonia ≥10 days in duration, diarrhea ≥10 days in duration, postmeasles croup, or transfer for intensive care.

§Refers to children who survived.

younger children (relative risk, 0.15; 95 percent confidence interval, 0.02 to 0.91). No child with a serum retinol concentration ≥0.7 μmol per liter (20 μg per deciliter) died, but the smallness of this group (n = 14) leaves the significance of the finding in doubt.

Discussion

The results of our randomized, controlled trial indicate a remarkable protective effect of vitamin A in severe measles, notwithstanding the provision of good general medical care and the presence of complicated advanced disease. Vitamin A reduced the death rate by more than half and the duration of pneumonia, diarrhea, and hospitalization by about one third. Vitamin A also appeared to reduce the incidence of herpes stomatitis and the need for intensive care. The consistency of benefit with respect to all measures of outcome is noteworthy, since mortality is not a sensitive criterion. Because of their reliance on mortality rates, previous studies of measles[5,6] lacked the statistical power to establish the benefit of vitamin A therapy.

The favorable response to vitamin A therapy may be understood in terms of the very high incidence (92 percent) of hyporetinemia in our patients (Table 2). Hyporetinemia implies a state of vitamin A deficiency at the tissue level, since there are virtually no peripheral-tissue stores of vitamin A except in the retina.[33-36] Serum retinol levels below 0.7 μmol per liter (20 μg per deciliter) appear to be inadequate for the body's biologic needs.[33] Oral vitamin A is absorbed well even in patients with diarrhea,[37] so the observed effects of treatment may reasonably be ascribed to correction of the tissue deficit of vitamin A. We do not know, however, whether the deficit was rectified by increases in the serum retinol concentration or by some other mechanism, since serum retinol levels were not measured after therapy.

Hyporetinemia appears almost invariable in children with severe measles,[8-11] as in this study, and the reduction in the serum retinol level is associated with increasingly severe disease.[11] Since many of these data come from populations in which nutritional vitamin A deficiency is a known problem,[8-10] it has been inferred that hyporetinemia in measles represents the exhaustion of hepatic stores.[6,7,20] There is a possible alternative mechanism, however. Hyporetinemia may occur in the presence of adequate hepatic stores of vitamin A when the stores are not mobilized fast enough to meet demand.[36] This has been found in fever, pneumonia, rheumatoid arthritis, hepatitis, acute tonsillitis, and rheumatic fever[36]; in protein-energy malnutrition[38]; and now also in measles.[8] Inadequate mobilization of hepatic stores may therefore underlie the hyporetinemia in children with severe measles from Kinshasa, Zaire,[11] and Cape Town, where nutritional vitamin A deficiency is uncommon. A study 25 years ago showed vitamin A deficiency to be rare in Cape Town, even in children with severe protein-energy malnutrition,[38] and it still appears to be rare. A search of the computer data-base listing of inpatients at our children's hospital, which predominantly serves the local underprivileged community, found only three instances of clinical vitamin A deficiency among 161,381 children admitted over a 13-year period, with no cases since 1985.

In view of the evidence that hyporetinemia may occur in the presence of adequate hepatic stores of vitamin A[38] and in populations not known to be deficient in vitamin A,[11] it would seem prudent to proceed on the assumption that previous nutritional adequacy may not ensure against the development of hyporetinemia in severe measles. For all children seriously ill with measles, vitamin A replacement should thus be provided at the dose given by Barclay et al.[9] (400,000 IU), which proved effective and safe in our study. A lower dose (100,000 to 200,000 IU) is recommended by the World Health Organization,[20] but its efficacy in measles has yet to be established.

It may be asked whether it is cost effective to advocate treatment with vitamin A for all children with

severe measles. Clearly, children under two years of age are at highest risk of an adverse outcome and derive the most benefit from vitamin A. When resources are scarce, such children should be given priority. In our study, however, half the children over two years of age were at risk of xerophthalmia because of serum retinol levels below 0.35 μmol per liter (10 μg per deciliter),[31] and hence they should have vitamin A prophylaxis. Thus, when resources permit, all children with severe measles should be given supplemental vitamin A.

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References

1. Grant JP. The state of the world's children, 1988. Oxford: Oxford University Press, 1988:3.
2. Foster A, Sommer A. Childhood blindness from corneal ulceration in Africa: causes, prevention, and treatment. Bull World Health Organ 1986; 64:619-23.
3. Warner JO, Marshall WC. Crippling lung disease after measles and adenovirus infection. Br J Dis Chest 1976; 70:89-94.
4. Kaschula RO, Druker J, Kipps A. Late morphologic consequences of measles: a lethal and debilitating lung disease among the poor. Rev Infect Dis 1983; 5:395-404.
5. Ellison JB. Intensive vitamin therapy in measles. BMJ 1932; 2:708-11.
6. Barclay AJG, Foster A, Sommer A. Vitamin A supplements and mortality related to measles: a randomised clinical trial. BMJ 1987; 294:294-6.
7. Vitamin A for measles. Lancet 1987; 1:1067-8.
8. Reddy V, Bhaskaram P, Raghuramulu N, et al. Relationship between measles, malnutrition, and blindness: a prospective study in Indian children. Am J Clin Nutr 1986; 44:924-30.
9. Inua M, Duggan MB, West CE, et al. Postmeasles corneal ulceration in children in northern Nigeria: the role of vitamin A, malnutrition and measles. Ann Trop Paediatr 1983; 3:181-91.
10. Varavithya W, Stoecker B, Chaiyaratana W, Kittikool J. Vitamin A status of Thai children with measles. Trop Geogr Med 1986; 38:359-61.
11. Markowitz LE, Nzilambi N, Driskell WJ, et al. Vitamin A levels and mortality among hospitalized measles patients, Kinshasa, Zaire. J Trop Pediatr 1989; 35:109-12.
12. Scrimshaw NS, Taylor CE, Gordon JE. Interactions of nutrition and infection. WHO monograph series no. 57. Geneva: World Health Organization, 1968.
13. Lassen HCA. Vitamin A deficiency and resistance against a specific infection: preliminary report. J Hyg (Lond) 1930; 30:300-10.
14. Milton RC, Reddy V, Naidu AN. Mild vitamin A deficiency and childhood morbidity — an Indian experience. Am J Clin Nutr 1987; 46:827-9.
15. Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory disease and diarrhea in children with preexisting mild vitamin A deficiency. Am J Clin Nutr 1984; 40:1090-5.
16. Sommer A, Tarwotjo I, Hussaini G, Susanto D. Increased mortality in children with mild vitamin A deficiency. Lancet 1983; 2:585-8.
17. Sommer A, Tarwotjo I, Djunaedi E, et al. Impact of vitamin A supplementation on childhood mortality: a randomised controlled community trial. Lancet 1986; 1:1169-73.
18. Green HN, Mellanby E. Vitamin A as an anti-infective agent. BMJ 1928; 2:691-6.
19. Reynolds LG, Hussey G, Kettles AN. Continuing scourge of measles. S Afr Med J 1987; 71:611.
20. Expanded programme on immunization: programme for the prevention of blindness nutrition. Joint WHO/UNICEF statement: vitamin A for measles. Wkly Epidemiol Rec 1987; 62:133-4.
21. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. Am J Clin Nutr 1979; 32:607-29.
22. Catignani GL, Bieri JG. Simultaneous determination of retinol and alpha-tocopherol in serum or plasma by liquid chromatography. Clin Chem 1983; 29:708-12.
23. Rosner B. Fundamentals of biostatistics. 2nd ed. Boston: Duxbury Press, 1986.
24. Siegel S. Nonparametric statistics for the behavioral sciences. New York: McGraw-Hill, 1956.
25. Greenland S, Robins JM. Estimation of a common effect parameter from sparse follow-up data. Biometrics 1985; 41:55-68.
26. Behrman RE, Vaughan VC III, Nelson WE. Nelson textbook of pediatrics. 13th ed. Philadelphia: W.B. Saunders, 1987.
27. Central Statistical Services, Pretoria. Population Census 1985. Report no. 02-85-02. Pretoria, South Africa: Government Printer, 1986.
28. Hugo-Hamman CT, Kibel MA, Michie CA, Yach D. Nutrition status of pre-school children in a Cape Town township. S Afr Med J 1987; 72:353-5.
29. Axton JH. Measles and the state of nutrition. S Afr Med J 1979; 55:125-6.
30. Morley D. Paediatric priorities in the developing world. London: Butterworths, 1973:207-30.
31. Vitamin A deficiency and xerophthalmia: Report of a joint WHO/USAID meeting. WHO Tech Rep Ser 1976; 590:1-88.
32. Kipps A, Kaschula RO. Virus pneumonia following measles: a virological and histological study of autopsy material. S Afr Med J 1976; 50:1083-8.
33. Olson JA. Vitamin A, retinoids, and carotenoids. In: Shils ME, Young VR, eds. Modern nutrition in health and disease. 7th ed. Philadelphia: Lea & Febiger, 1988:292-312.
34. Pitt GA. The assessment of vitamin A status. Proc Nutr Soc 1981; 40:173-8.
35. Olson JA. Metabolism of vitamin A. Biochem Soc Trans 1986; 14:928-30.
36. Barker BM. Vitamin A. In: Barker BM, Bender DA, eds. Vitamins in medicine. Vol. 2. 4th ed. London: Heinemann, 1983:211-90.
37. Molla A, Islam A, Molla AM, Jahan F. Change in serum vitamin A concentration after an oral dose in children with diarrhea. J Pediatr 1983; 103:1000-2.
38. Konno T, Hansen JD, Truswell AS, Woodd-Walker R, Becker D. Vitamin-A deficiency and protein-calorie malnutrition in Cape Town. S Afr Med J 1968; 42:950-5.

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Research from the South

Vitamin A supplements and mortality related to measles: a randomised clinical trial

ANDREW J G BARCLAY, ALLEN FOSTER, ALFRED SOMMER

Abstract

One hundred and eighty children admitted with measles were randomly allocated to receive routine treatment alone or with additional large doses of vitamin A (200 000 IU orally immediately and again the next day). Baseline characteristics of the two groups were virtually identical for age, severity of measles, and vitamin A and general nutritional states. In 91% of the children serum vitamin A concentrations were less than 0·56 umol/l. Of the 88 subjects given vitamin A supplements, six (7%) died; of the 92 controls, 12 (13%) died (p=0·13). This difference in mortality was most obvious for children aged under 2 years (one death out of 46 children receiving supplements versus seven deaths out of 42 controls; p<0·05) and for cases complicated by croup or laryngotracheobronchitis. Mortality was several times higher in marasmic than in better nourished children, regardless of study allocation (p<0·01).

Introduction

Recent reports from Indonesia have shown that children with clinically mild vitamin A deficiency have a fourfold increase in mortality from all causes[1] and a threefold increase in the incidence of respiratory and diarrhoeal diseases.[2] Vitamin A supplements reduced preschool age childhood mortality by over 30%.[3] After reviewing some 50 reports of the effect of vitamin A deficiency on bacterial, viral, protozoal, and helminthic infections in man and animals Scrimshaw *et al* concluded that "no nutritional deficiency is more consistently synergistic with infectious disease than that of vitamin A."[4] At the time that they wrote this they were unable to find data concerning the interaction between vitamin A and measles.

Vitamin A is essential for the maintenance of normal epithelial tissues throughout the body. In the absence of vitamin A mucosal epithelium undergoes squamous metaplasia, with a concomitant decrease in cell turnover.[5,6] Measles is a viral disease that infects and damages epithelial tissues throughout the body.[10,11] The disease can also decrease serum concentrations of vitamin A in well nourished children to less than those observed in non-infected malnourished children.[12] Measles probably increases utilisation of vitamin A, and children with marginal liver stores of the vitamin may thus develop acute vitamin A deficiency, resulting in eye damage and possibly increased mortality from respiratory and diarrhoeal causes. Indeed, measles is an important risk factor in the development of severe vitamin A deficiency and xerophthalmia in Asia.[13,14] It is also a particularly virulent disease among African children, accounting for most cases of childhood blindness and for considerable mortality.[6,11,15,16] Recent data suggest that vitamin A deficiency may be prevalent in areas of Africa, including Tanzania.[16,18,19]

This hospital based study sought to determine the effect of high dose vitamin A supplements taken during early infection with measles on subsequent mortality in African children.

Patients and methods

Mvumi Hospital is a rural general hospital in central Tanzania related to the church. Paediatric patients are drawn almost entirely from the local population, which comprises subsistence farmers living in a fairly arid environment. The staple diet is millet eaten with a green vegetable relish.

There is only one harvest a year, in April to May, and that is dependent on good rains. The rains in 1982 were very bad, leaving conditions of near famine for many, but the rains and harvest in 1983 were good. Malnutrition is a great problem in children. About a quarter of all children admitted are severely malnourished, and only 30% have a weight for age above 80% of the standard.[20] Anaemia is also common. The general paediatric background is more fully described elsewhere (A J G Barclay, unpublished).

We attempted to include in this study every child with measles presenting to the hospital from September 1982 to November 1983, a period that included an entire measles season. Measles was diagnosed on clinical grounds that included a history of prodromal disease and the presence of a typical rash. On admission all children were given a full clinical examination by the paediatrician. Shortly after admission they were seen by a member of the eye department. They were all weighed and measured by the nurses and had their haemoglobin concentration measured and a blood slide examined by staff in the hospital laboratory.

A venous blood sample was taken on admission for estimation of vitamin A state. Half of the subjects were then randomly allocated to receive vitamin A (200 000 IU in oil orally immediately and again the next day); the other children were given standard treatment. Randomisation was accomplished by sequential assignment of single digits from a random numbers table, odd digits dictating one group and even the other. Which children received vitamin A was known to the paediatrician but not recorded in the general notes: study allocation was therefore not known by any other staff dealing with care of the children. Other main therapeutic sources of vitamin A—for example, multivitamins—are not routinely given and therefore were not received by any children in the trial. The two groups were treated identically in the ward, fed the same diet, and given antibiotics or further investigated as indicated by their clinical condition.

Deaths caused by measles were taken to be deaths occurring within one month of onset of the rash. Most patients were still in the ward when they died; three returned of their own accord and were readmitted with dysentery or diarrhoea and died quickly and two ran away moribund and died at home.

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Baseline blood samples were allowed to clot and were then spun down. The serum was separated and stored in a deep freeze within four hours of taking the sample. The serum was later shipped to Baltimore, where concentration of vitamin A (as retinol) was measured by high performance liquid chromatography.[21] Because of losses in transport biochemical determinations are available for only 38 recipients of vitamin A and 17 controls.

As the study was designed to assess the beneficial impact of vitamin A supplements, and there was no biological, clinical, or epidemiological reason to suspect any deleterious effects from added vitamin A, results were assessed with a single tail normal deviate (z) and Fisher's exact test.

Results

Two hundred and twelve patients with measles were admitted during the trial. Thirty two were excluded from the trial, all but six before randomisation because of corneal ulcers (seven patients, who were automatically given vitamin A and are reported on separately[22]); death within 24 hours of admission (five); running away within 24 hours (one); receiving vitamin A before admission (nine); and admission while the study coordinator was absent (10). Of the 180 children in the trial, 11 did not have their height recorded and 15 did not have their haemoglobin concentration measured.

The distribution of baseline characteristics of recipient and control children was similar, including age (mean recipient 29·5 v mean control 30·7 months), weight for age (72% v 75% of standard), weight for height (83% v 86% of standard), haemoglobin concentration (85 v 89 g/l), interval between onset of rash and admission (3·5 v 3·4 days), and serum vitamin A concentration (0·30 v 0·32 umol/l). Only 9% of patients had serum vitamin A concentrations greater than 0·53 umol/l.

Of the 88 children given vitamin A, six (7%) died (table I). Of the 92 controls, 12 (13%) died. Despite the large clinical difference small numbers limit its significance ($p=0·13$). The difference was most obvious for children aged under 2 years ($p<0·05$).

TABLE I—*Mortality of children admitted with measles*

Age (months)	No of children admitted		No (%) who died	
	Given vitamin A	Controls	Given vitamin A	Controls
<9	14	9		2 (22)
9-11	12	10		2 (20)
12-23	20	23	1 (5)	3 (13)
24-35	11	16	3 (27)	2 (13)
36-47	11	13	1 (9)	1 (8)
48-59	8	6	1 (13)	
≥60	12	15		2 (13)
Total	88	92	6 (7)	12 (13)

Twenty five children (14%) were marasmic, and 104 (58%) were underweight as assessed by weight for age (table II). The mortality of marasmic children was several times higher than that of better nourished children, regardless of whether they had received vitamin A or not ($p<0·01$, two tailed test). In every nutritional category mortality was lower for vitamin A recipients.

Complications, usually already present at the time of admission, were equally common in the two groups, but mortality from such complications was higher in the control group (table III). Pneumonia was the commonest complication, affecting 85 children. Croup complicated measles in 13 of the control group, of whom four (31%) died; in contrast, of eight children with croup given vitamin A, none died. Very few children had dysentery; of those who did, half died.

TABLE II—*Weight for age and mortality*

Weight for age*	No of children in study		No (%) who died		
	Given vitamin A	Controls	Given vitamin A	Controls	Total
>80%	24	27	1 (4)	3 (11)	4 (8)
60-80%	47	57	1 (2)	6 (11)	7 (7)
<60%	17	8	4 (24)	3 (38)	7 (28)
Total	88	92	6 (7)	12 (13)	18 (10)

*Percentage of median National Center for Health Statistics standard.[19]

TABLE III—*Complications and associated mortality*

Complication	No (%) of children with complications		No (%) of children who died	
	Given vitamin A	Controls	Given vitamin A	Controls
Pneumonia	38 (43)	47 (51)	3 (8)	7 (15)
Otitis media	19 (22)	20 (22)	1 (5)	3 (15)
Croup or laryngotracheobronchitis	8 (9)	13 (14)		4 (31)
Dysentery	2 (2)	6 (7)	1 (50)	3 (50)
Haemorrhagic rash	28 (32)	34 (37)	1 (4)	4 (12)
Oral candidiasis	9 (10)	5 (5)	1 (11)	1 (20)

Discussion

Children randomised to receive vitamin A did not differ from the control group in baseline age, nutritional state, duration of illness, prevalence of complications, or haemoglobin or serum vitamin A concentrations. Mortality was twice as high in the control group as in the treated group, almost all of the difference being accounted for by children aged under 2 years ($p<0·05$).

Although the numbers were small, there was a remarkable consistency in the beneficial impact of vitamin A supplements on complicating illness and nutritional strata. This was especially obvious among children with croup or laryngotracheobronchitis. No child who received vitamin A died of laryngotracheobronchitis, whereas four in the control group died. Laryngotracheobronchitis is a particularly difficult condition to treat with limited resources. Because repair of epithelial surfaces in children with early vitamin A deficiency may be poor, with a tendency to develop into squamous metaplasia of the respiratory tract,[23] they may suffer increased susceptibility to laryngotracheobronchitis or its consequences.

Malnutrition is common in and around Mvumi, and the nutritional state of this study group is not atypical of general paediatric admissions. Children with low weight for age (and weight for height, not shown) had the highest mortality in both study groups. Recent community studies have shown a varying relation between premorbid general nutritional state and death from measles, but most dealt with milder disease.[24-26] Schrimshaw *et al* noted a decrease in mortality from measles in children fed a vegetable extract rich in protein that may have contained considerable amounts of vitamin A.[27] In our study vitamin A recipients suffered lower mortality in every nutritional stratum.

The vitamin A concentrations among the children in our study were all very low, much lower than that reported by workers in Nigeria.[12] This is explained partly by the different analytical methods, populations, and diet. Tielsch and Sommer found that children with vitamin A concentrations of less than 0·53 umol/l, a category that would include over 90% of our study group, were at very high risk of developing corneal ulcers.[11]

Vitamin A deficiency may be a large factor in determining the outcome of measles in Africa, just as it seems to affect morbidity and mortality in Asia.[1-3] When a child with marginal vitamin A stores gets measles available vitamin A is quickly depleted, presumably reducing the ability to resist secondary infections or their consequences, or both.[28-32] This would exacerbate the already reduced immunocompetence thought to be associated with measles infection.[33]

Further trials in different parts of Africa are urgently needed to define the role of vitamin A deficiency in measles morbidity and mortality and the importance of vitamin A supplements in their control.

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References

1 Sommer A, Hussaini G, Tarwotjo I, Susanto D. Increased mortality in children with mild vitamin A deficiency. *Lancet* 1983;ii:585-8.
2 Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory disease and diarrhoea in children with pre-existing mild vitamin A deficiency. *Am J Clin Nutr* 1984;40:1090-5.
3 Sommer A, Tarwotjo I, Djunaedi E, *et al.* Impact of vitamin A supplementation on childhood mortality: a randomized controlled community trial. *Lancet* 1986;i:1169-73.
4 Scrimshaw NS, Taylor CE, Gordon JE. Interaction of nutrition and infection. *WHO Monogr Ser* 1968;No 57.
5 Wolbach SB, Howe PR. Tissue changes following deprivation of fat-soluble A vitamin. *J Exp Med* 1925;42:753-77.
6 Blackfan KD, Wolbach SB. Vitamin A deficiency in infants: a clinical and pathological study. *J Pediatr* 1933;3:679-706.
7 Sweet LK, K'ang HJ. Clinical and anatomic study of avitaminosis A among the Chinese. *Am J Dis Child* 1935;50:699-734.
8 Fell HB, Mellanby E. Metaplasia produced in tissue cultures of chick ectoderm by high vitamin A. *J Physiol* 1953;119:470-88.
9 Olson JA. The biological role of vitamin A in maintaining epithelial tissues. *Int J Med Sci* 1972;1:1170-8.
10 Morley D. Severe measles in the tropics I. *Br Med J* 1969;ii:297-300.
11 Morley D. Severe measles in the tropics II. *Br Med J* 1969;ii:363-5.
12 Inua M, Duggan MB, West CE, *et al.* Post measles corneal ulceration in children in northern Nigeria: the role of vitamin A, malnutrition and measles. *Ann Trop Paediatr* 1983;3:181-91.
13 Sommer A. *Nutritional blindness: xerophthalmia and keratomalacia.* New York: Oxford University Press, 1982.
14 Tielsch JM, Sommer A. The epidemiology of vitamin A deficiency and xerophthalmia. *Annu Rev Nutr* 1984;4:183-205.
15 Chirambo MC, Ezra DB. Causes of blindness among students in blind school institutions in a developing country. *Br J Ophthalmol* 1976;60:665-8.
16 Sauter JJM. *Xerophthalmia and measles in Kenya.* Groningen: Drukkerij van Denderen, 1976.
17 Chirambo MC, Tielsch JM, West KP, *et al.* Blindness and visual impairment in southern Malawi. *Bull WHO* (in press).
18 Tielsch JM, West KP, Katz J, *et al.* Prevalence and severity of xerophthalmia in southern Malawi. *Am J Epidemiol* (in press).
19 Foster A, Kavishe F, Sommer A, Taylor HR. A simple surveillance system for xerophthalmia and childhood corneal ulceration. *Bull WHO* (in press).
20 Hamill PVV, Drizd TA, Johnson CL, *et al. NCHS growth curves for children, birth-18 years, United States.* Hyattsville, Maryland: National Center for Health Statistics, 1977 (DHEW publication No PHS 78-1650).
21 Bieri JG, Tolliver TJ, Catignani GL. Simultaneous determination of alpha-tocopherol and retinol in plasma or red cells by high pressure liquid chromatography. *Am J Clin Nutr* 1979;32:2143-49.
22 Foster A, Sommer A. Corneal ulceration, measles and childhood blindness in Tanzania. *Br J Ophthalmol* (in press).
23 Muller AS, Voornoeve AM, Manneije W, Schupen TWJ. The impact of measles in a rural area of Kenya. *East Afr Med J* 1977;54:364-72.
24 Koster FT, Curlin GC, Aziz KMA, Haque A. Synergistic impact of measles and diarrhoea on nutrition and mortality in Bangladesh. *Bull WHO* 1981;59:901-8.
25 Aaby P, Bukh J, Lisse IM, Smits AJ. Measles mortality, state of nutrition and family structure: a community study from Guinea-Bissau. *J Infect Dis* 1983;147:693-701.
26 Aaby P, Bukh J, Lisse IM, *et al.* Determinants of measles mortality in a rural area of Guinea-Bissau: crowding, age, and malnutrition. *J Trop Pediatr* 1984;30:164-8.
27 Scrimshaw NS, Salmon JB, Bruch HA, Gordon JE. Measles, diarrhoea and nutritional deficiency in rural Guatemala. *Am J Trop Med Hyg* 1966;15:625-31.
28 Beaver DL. Vitamin A deficiency in the germ-free rat. *Am J Pathol* 1961;38:335-49.
29 Rogers WE, Bieri JG, McDaniel EG. Vitamin A deficiency in the germ free state. *Fed Proc* 1971;30:1773-8.
30 Kochanowski BA, Ross AC. Stimulation of humoral immunity by vitamin A during suckling and postweaning in the rat. *J Nutr* (in press).
31 Nauss KM, Mark DA, Suskind RM. The effect of vitamin A deficiency in the in vitro cellular immune response of rats. *J Nutr* 1979;109:1815-23.
32 Bhaskaram C, Reddy V. Cell-mediated immunity in iron and vitamin deficient children. *Br Med J* 1975;iii:522.
33 Whittle HC, Sandford-Smith J, Koube OI, Dossetor J, Duggan M. Severe ulcerative herpes of mouth and eye following measles. *Trans R Soc Trop Med Hyg* 1979;73:66-9.

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Guide pour les programmes de soins de santé primaires

PRISE EN CHARGE DE LA ROUGEOLE ET LA VITAMINE A

Introduction

On peut aisément prévenir la rougeole grâce à la vaccination. En dépit de cela, en 1989, 45 millions d'enfants ont souffert de cette maladie dans les pays en développement : 1,4 millions d'entre eux en sont morts. La mortalité attribuable à la rougeole est principalement le résultat de complications telles que la pneumonie, la diarrhée ou le croup. Il est d'autres complications de la rougeole, telles que la cécité, l'antrite, l'encéphalite et les perturbations de la croissance qui provoquent des incapacités à vie. En Afrique seulement, où la prévalence de la cécité chez les enfants d'âge préscolaire est estimée à 1/1000, on estime que la rougeole est la cause de la moitié des cas de cécité chez l'enfant. L'incidence de la mortalité et de la morbidité (attribuables à d'autres maladies de l'enfance) dans les mois qui suivent l'apparition de la rougeole peut être dix fois supérieure chez les sujets qui ont survécu à la rougeole. Cette incidence plus durable, ne commence à être perçue que maintenant, ce qui signifie que les répercussions néfastes de la maladie sont plus graves qu'on ne le pensait.

Pour l'heure, il n'y a pas de cure ou de traitement spécifique contre la rougeole elle-même. Par conséquent les lignes directrices établies pour lutter contre cette maladie visent essentiellement la prévention et le traitement de ses complications : antibiotiques pour les infections secondaires, antipyrétiques contre la fièvre, réhydratation orale contre la diarrhée et soins ophtalmologiques contre les complications oculaires. Des études récemment réalisées en Afrique montrent que la thérapeutique à base de vitamine A réduit les risques de mortalité et les complications des cas de rougeole aiguë de moitié. Bien que la vitamine A n'ait pas d'effet direct sur le virus de la rougeole, elle prévient ou réduit la gravité des complications, théoriquement grâce à son rôle de protection du système immunitaire et du tissu épithélial. La rougeoie réduit le niveau de vitamine A sérique, causant ainsi un état de carence qui n'est pas forcément visible à l'issue d'un examen clinique. On pense que le fonctionnement du revêtement épithélial de l'oeil et des voies respiratoires et gastro-intestinales est perturbé lorsque les niveaux de vitamine A sérique tombent et se maintiennent en dessous de certains niveaux critiques. En effet, le virus de la rougeole et d'autres agents pathogènes envahissent alors ces tissus en causant des lésions oculaires, la diarrhée, la pneumonie, le croup et l'antrite.

La vitamine A peut se révéler fort efficace dans la réduction de la mortalité et des complications attribuables à la rougeole, lorsqu'elle est administrée oralement sous forme de liquide concentré en capsule ou en flacon. Aucun savoir-faire technique, aucun équipement particulier n'est nécessaire. Etant donné que les impératifs techniques et opérationnels du traitement de la rougeole à base de vitamine A sont peu nombreux, ce traitement peut facilement être ajouté aux techniques de lutte déjà en place. Chaque programme devra adapter la composante vitamine A pour qu'elle puisse s'inscrire dans les politiques et pratiques en vigueur. De manière plus précise, les mesures suivantes devraient être prises :

- Publication de lignes directrices nouvelles ou révisées sur le traitement des cas de rougeole.
- Formation du personnel sanitaire (agents de santé, superviseurs, formateurs, responsables) sur les raisons d'être et les modalités du traitement de la rougeole par le biais d'une brève formation sur le tas.
- Acquisition et distribution de stocks, notamment de vitamine A.
- Compléments d'information aux rapports et formulaires existants pour assurer un suivi efficace du traitement des cas de rougeole.

Il convient de souligner que l'administration de vitamine A pour les cas de rougeole ne devrait pas faire oublier l'importance de la vaccination univer-

selle, de l'amélioration de la situation nutritionnelle ou des traitements appropriés des complications de la rougeole. En fait, la principale intervention de lutte efficace et durable contre la rougeole est la vaccination universelle. En préservant un bon état nutritionnel chez les enfants de 6 à 24 mois, on peut assurer une réduction des cas de mortalité attribuables à la rougeole et ***à d'autres maladies courantes de l'enfance***. L'expérience clinique révèle cependant que l'on peut enregistrer une réduction spectaculaire de la mortalité liée à la rougeole si tous les enfants qui souffrent de cette maladie reçoivent des compléments vitaminiques A administrés par voie orale. Les coûts en sont minimes.

Le présent dossier contient certains instruments qui faciliteront l'adoption, dans le cadre de programmes existants, de nouvelles connaissances sur les interventions nutritionnelles — en particulier les compléments vitaminiConseillers techniques :Conseillers techniques :ques A - contre la rougeole. L'on a présupposé que les utilisateurs de ce dossier sont familiarisés avec les lignes directrices de vaccination contre la rougeole et les techniques de traitement de la maladie et de ses complications. C'est pourquoi il porte essentiellement sur des informations nouvelles relatives aux interventions contre la rougeole, et en particulier à l'utilisation de la vitamine A en insistant particulièrement sur l'alimentation.

Le présent dossier contient les éléments suivants :

- **Prise en charge de la rougeole**
  Utile pour les agents de santé à tous les niveaux. Il résume tous les aspects des interventions contre les cas de rougeole, depuis le diagnostic jusqu'au traitement.

- **Prise en charge de la rougeole et la vitamine A : légendes de diapositives**
  Contient certaines informations pratiques dont ont besoin les agents de santé et leurs supérieurs hiérarchiques. On y explique comment mettre en oeuvre les nouvelles lignes directrices relatives aux compléments vitaminiques A dans le cadre d'un programme complet de lutte contre la rougeole.

- **Approvisionnement en vitamine A : lignes directrices**
  Utile pour les employés chargés de la commande des fournitures et de la gestion des stocks.

- **Les fondements scientifiques de l'utilisation de la vitamine A : bibliographie**
  Contient des informations techniques pour les médecins, les chercheurs et les responsables dotés d'une formation technique.

Conseillers techniques :

Jesús Bulux, CESSIAM, Guatemala
David Calder, Bureau de développement régional, AID, Suva
Moses Chirambo, Représentant Afrique de Sight Savers, Lilongwe
Nicholas Cohen, OMS/PEV, Genève
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1. Diagnostic de la rougeole

Il n'y a pas de test rapide de laboratoire pour le diagnostic de la rougeole. On peut poser la définition suivante pour les cas cliniques simples de rougeole :

> **Fièvre pendant plus de trois jours avec une éruption maculo-papulaire caractéristique et au moins l'un des symptômes suivants : toux, nez qui coule, rougissement des yeux.**

Pour établir un diagnostic des complications de rougeole , il faut suivre deux étapes : établir un historique après l'apparition des premiers signes et procéder à un examen clinique conformément à ce qui suit :

Historique

— Questions à poser :

1. Allaitement, et si l'enfant mange des aliments de sevrage.
2. Est-ce que l'enfant peut boire?
3. Toux, respiration rapide et difficile : symptômes de pneumonie.
4. Diarrhée : c'est-à-dire au moins trois selles sans consistance par jour.
5. Sécrétions des yeux ou des oreilles : symptômes de conjonctivite ou d'antrite.
6. Changements dans l'état de conscience : peut être attribuable à la déshydratation ou à l'encéphalite ou peut tout simplement être un symptôme d'un enfant gravement malade.

Examen clinique

—A vérifier en particulier :

1. Température.
2. Poids : si possible, inscrire le poids sur un tableau de croissance. Si le poids a été préalablement relevé, une perte pondérale peut être un signe de déshydratation et de malnutrition.
3. Signes de déshydratation : membranes muqueuses sèches, perte d'élasticité de la peau, instabilité psychomotrice.
4. Taux de respiration et tirage : respiration rapide et tirage sont des signes de pneumonie aiguë.
5. Lésion de la cornée : la partie centrale de l'oeil est normalement claire et noire mais elle peut devenir opaque ou être endommagée.
6. Sécrétion auriculaires : elle ne peut être visible qu'à l'issue d'un examen.
7. La bouche — pour des ulcères.

2. Conseils aux mères

L'enfant sera faible et sujet à infections pendant un certain temps. Dans les cas de rougeole sans complication, la fièvre tombe en l'espace d'une semaine et les éruptions disparaissent au bout de 10 à 14 jours. Cela dit, la vulnérabilité aux maladies et à la mort peut persister pendant un an après la rougeole. On devrait encourager les mères à chercher un traitement dès que possible.

- **Continuer à allaiter** ou donner à l'enfant autant d'aliments de sevrage et de liquides le plus souvent possible. Pendant la période de récupération qui suit la rougeole il importe de lui donner des aliments fortement énergétiques faciles à assimiler, des fruits et légumes "jaunes" ainsi que des légumes verts.

- **Surveiller la fièvre** afin de réduire les risques de convulsion en préservant une température aussi normale que possible.

- **Faire suivre un traitement à l'enfant** si :

  1. Son état général empire.
  2. Sa respiration s'accélère ou devient difficile.
  3. La diarrhée persiste ou des signes de déshydratation apparaissent.
  4. L'enfant ne peut pas boire.
  5. Il commence à avoir mal aux yeux, ces derniers deviennent nébuleux ou sa vision commence à s'altérer.

3. Dosage de la vitamine A

La vitamine A permet de sauver la vie durant les étapes aiguës de la rougeole. Elle réduit en outre la gravité de nombreuses complications à long terme. Il convient d'administrer de la vitamine A à tous les enfants ayant la rougeole :

- Dans les régions où la mortalité attribuable à la rougeole est réputée être élevée.[1]

- Dans les régions qui sont réputées souffrir de carences vitaminiques A.[1]

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1 (NOTE ED. : Toutes les communautés rurales et urbaines à faibles revenus des pays en développement ont beaucoup plus de risques de tomber dans ces catégories. Les études permettant de déterminer la mortalité causée par la rougeole et la prévalence des carences vitaminiques A sont coûteuses et techniquement complexes. Les responsables de programmes de santé primaire doivent eux-mêmes décider s'il est opportun d'investir dans la réalisation de ces études lorsqu'il n'y a pas de données récentes disponibles, ou s'il convient plutôt d'administrer deux doses de vitamine A en supposant que la situation présentée plus haut risque fort de prévaloir dans les communautés en question.)

- Dans n'importe quel cas de rougeole aiguë ou compliquée. Les compléments de vitamine A devraient être administrés aux enfants souffrant de rougeole aiguë même dans les pays industrialisés tels que les Etats-Unis ou les pays d'Europe.

Les compléments de vitamine A sont disponibles en capsules (50 000, 100 000 ou 200 000 IU) ou sous forme de liquide dans un flacon. Il convient de lire les instructions figurant sur les étiquettes avant d'administrer. Dans le cas des enfants de moins de deux ans, il est nécessaire d'ouvrir les capsules. Les capsules présentent cet avantage en ce sens qu'elles peuvent être distribuées aux mères pour qu'elles puissent ensuite les administrer à la maison.

- Administrer directement à l'enfant la première dose de vitamine A.

VITAMINE A EN CAS DE ROUGEOLE

	Dès le diagnostic	Lendemain
Enfants de moins de 12 mois	100,000 IU	100,000 IU
Enfants d'au moins un an	200,000 IU	200,000 IU

- Veiller à ce que la mère comprenne bien les instructions si elle est censée donner la deuxième dose à la maison. S'assurer qu'elle comprend bien qu'il est nécessaire que l'enfant reçoive une seconde dose le lendemain.

4. S'informer sur la vaccination

Poser des questions sur la situation de l'enfant, et des autres enfants au foyer, en matière de vaccination. Chaque contact est une occasion de mettre à jour le carnet de vaccination de l'enfant et de lui administrer des rappels.

5. Diagnostic des complications

Un enfant souffrant de rougeole aiguë ou de complications aura besoin d'un traitement particulier. Dans certains cas, l'enfant devra être orienté en conséquence. On considère que l'enfant souffre de rougeole aiguë ou de complications s'il présente l'un des symptômes énumérés dans l'encadré ci-dessous.

SYMPTOMES	DIAGNOSTIC
Perte de poids récente et considérable	Déshydratation et/ou malnutrition
Toux avec respiration rapide ou Tirage	Pneumonie
Au moins trois selles sans consistance par jour	Diarrhée
Partie centrale de l'oeil opaque	Lésion oculaire avec risque de cécité
Sécrétion auriculaire	Antrite
Convulsions, coma	Encéphalite

6. Traitement des complications

Nombreuses sont les complications qui accompagnent les cas de rougeole aiguë. Les lignes directrices ci-dessous ne prétendent faire face qu'à celles qui sont les plus courantes. On citera notamment la malnutrition, la pneumonie, la diarrhée, les lésions oculaires et l'antrite. Les complications peuvent être complètement traitées. Si elles sont détectées suffisamment tôt, presque tous les enfants peuvent arriver à une pleine récupération.

6.1 Fièvre

1. Le paracétamol est le moyen le plus efficace de combattre la fièvre. En donner à l'enfant lorsqu'il a très chaud ou que sa température (prise à l'aisselle) est de 39$. Le pacétamol a moins d'effets secondaires que l'aspirine.

2. Lorsque l'enfant a des convulsions attribuables à la fièvre, on peut faire baisser sa température avec des compresses d'eau froide. On peut en outre lui administrer du paracétamol toutes les 4 à 6 heures.

NOTE : la fièvre à elle seule ne justifie pas un traitement aux antibiotiques.

6.2 Malnutrition

Les enfants ayant la rougeole commencent à souffrir de malnutrition pour les raisons suivantes :

- Ils perdent l'appétit à cause de la fièvre et de l'état de malaise général.
- Ils peuvent avoir du mal à manger à cause de douleurs à la bouche.
- L'assimilation des aliments est réduite à cause de la diarrhée.
- La demande en nutriments, quels qu'ils soient, s'accentue durant les phases aiguë et de récupération.
- Il est une erreur fort répandue qui consiste à ne plus donner à manger(au moins) aux enfants qui ont la rougeole.

Les enfants qui souffrent de complications suite à une rougeole doivent **non seulement** prendre suffisamment de liquides **mais également** avoir une ration alimentaire de qualité. Les mesures à prendre face à la malnutrition dépendent du degré de cette dernière et de l'âge de l'enfant. Les lignes directrices suivantes sont recommandées pour les enfants souffrant d'une malnutrition aiguë :

1. Encourager les mères à continuer d'allaiter.
2. Alimenter l'enfant à intervalles réguliers, au moins toutes les deux heures si possible.
3. Dans le cas des nourrissons et des enfants souffrant d'une malnutrition aiguë, commencer par 125 ml de lait moitié dilué par kilogramme de poids. A mesure que l'enfant regagne de l'appétit, la proportion peut être augmentée à 150 ml/kg, et cette fois de lait non dilué.
4. Ajouter de l'huile végétale et du sucre au lait ou aux préparations de sevrage afin d'accroître leur contenu énergétique.

En cas d'hospitalisation, peser l'enfant tous les jours pour suivre ses progrès. Le gain pondéral durant la phase de réhydratation intensive peut être marqué. Après la réhydratation, le "rattrapage" de la croissance devrait continuer d'être très rapide chez les enfants qui ont reçu une alimentation à forte teneur énergétique. Chez les enfants souffrant d'une malnutrition particulièrement grave, l'emploi d'un tube naso-gastrique peut être déterminant pour leur survie.

POUR DE PLUS AMPLES DETAILS VOIR : *Le Traitement et la Prise en Charge de la Malnutrition Protéine-Energétique Aiguë*, Organisation Mondiale de la Santé, Gèneve, 1981.

6.3 Pneumonie

Diagnostic

- La toux et l'accélération de la respiration sont des symptômes de la **pneumonie**. L'enfant doit être calme pour pouvoir écouter sa respiration.

- La toux, l'accélération de la respiration et le tirage sont des symptômes de la **pneumonie aiguë**. Par accélération de la respiration, on entend au moins 50 respirations par minute chez un enfant de 2 à 12 mois et au moins 40 respirations par minute chez un enfant de 12 mois à 5 ans. Le tirage est un net renfoncement de la paroi thoracique apparent entre les côtes, lorsque le sujet aspire.

- Lorsque la **pneumonie est particulièrement aiguë** l'enfant peut être incapable de boire. On peut également détecter une couleur bleutée aux lèvres et à la bouche (cyanose centrale), signe d'un manque d'oxygène dans le sang.

Traitement

1. Traitement de la pneumonie à la maison avec un antibiotique oral tel que le cotrimoxazole, l'amoxyciline ou l'ampicilline.
2. Recommander aux mères de revenir en consultation si la situation s'aggrave et si la respiration devient plus rapide ou difficile.
3. Si la pneumonie est particulièrement grave, hospitaliser si possible pour l'administration d'antibiotiques intramusculaires ou intraveineux.
4. Les enfants souffrant d'une pneumonie aiguë devraient, s'il y en a, recevoir de l'oxygène.
5. Le râle dû à la pneumonie peut également être traité aux antibiotiques. Ne pas employer de bronchodilatateurs tels que le salbutamol. Ne pas employer des stéroïdes pour traiter les râles.

6.4 Croup

Diagnostic

- Le croup se traduit par un bruit rauque lorsque le sujet aspire. Il est causé par une inflammation du larynx, de la trachée ou de l'épiglotte.

- Le croup se caractérise par un bruit particulièrement fort pendant la respiration alors que l'enfant est calme, des signes de tirage et un enrouement. Le danger du croup tient à ce que la respiration peut être gravement obstruée.

Traitement

1. Les cas de croup aiguë sont traités avec des antibiotiques. Employer du chloramphénicol si disponible.

2. Les cas de croup aiguë sont à traiter d'urgence. Administrer immédiatement un antibiotique même si l'enfant va être hospitalisé.

POUR DE PLUS AMPLES DETAILS VOIR : *Infections Respiratoires Aiguës chez l'Enfant : Traitement dans de Petits Hopitaux dans des Pays en Développement. Manuel Pour Médecins et Agents de Santé . Organisation Mondiale de la Santé, Genève, 1990.*

6.5 Diarrhée et déshydratation

Les trois règles du traitement de la diarrhée :

1. Donner à l'enfant plus de liquides que d'habitude afin de prévenir la déshydratation.
2. Faire manger l'enfant avec abondance pour éviter la sous-nutrition. Encourager la mère à continuer d'allaiter.
3. Si l'état de l'enfant ne s'améliore pas au bout de trois jours, ou si l'une des conditions suivantes se produit :

   —augmentation du nombre de selles liquides

   —omissements répétés

   —coif marquée

   —sang dans les selles emmener l'enfant au dispensaire.

Si l'enfant reçoit une solution de réhydratation orale (SRO) à la maison :

- Indiquer à la mère quelles quantités elle doit administrer après chaque selle suspecte et lui donner suffisamment de sachets pour deux jours.
- Montrer à la mère comment mélanger et administrer la SRO.
- Donner une petite cuillerée de SRO toute les 1 à 2 minutes à un enfant de moins de 2 ans et des gorgées fréquentes à un enfant plus âgé.
- Si l'enfant vomit, attendre 10 minutes, puis continuer à lui administrer la SRO, mais plus lentement.

Comment traiter rapidement les cas de déshydratation grave

- **Si vous avez été formé pour administrer des liquides par voie intraveineuse**, commencer immédiatement. Si l'enfant peut boire, lui donner de la SRO par voie orale pendant que le dispositif intraveineux est installé. Vérifier l'état de l'enfant toutes les heures ou toutes les deux heures. Si aucune amélioration n'est apparente accélérer le débit de l'intraveineuse.

- **Si vous ne pouvez pas administrer de liquides par voie intraveineuse**, administrez une solution SRO (20 ml/kg de poids) avec un tube naso-gastrique.

- **Si aucune de ces deux solutions n'est possible**, hospitaliser immédiatement.

En cas de traces de sang dans les selles :

Administrer pendant cinq jours un antibiotique oral recommandé contre les shigella dans votre région.

POUR DE PLUS AMPLES DETAILS VOIR : *Manuel pour le Traitement de la Diarrheé pour l'emploi des Médecins et Agents de Santé . Organisation Mondiale de la Santé, Genève, 1990.*

6.6 Lésions oculaires

Conjonctivite (yeux rouges ou collés) :

Apprendre à la mére à :

1. Nettoyer les yeux de l'enfant avec du coton ou un morceau de linge propre.
2. Administrer un collyre à base de tétracycline trois fois par jour pendant sept jours. La mère devrait :
   - Se laver les mains avant d'appliquer le produit et après avoir terminé.
   - Abaisser la paupière inférieure pour faire apparaître la conjonctive.
   - Placer une faible quantité sur le bord de la conjonctive inférieure.
   - Maintenir l'oeil de l'enfant fermé pendant au moins deux minutes.
3. Eviter d'employer d'autres remèdes.

Lésions de la cornée :

1. Administrer immédiatement des compléments vitaminiques A (deux doses séparées de 24 heures comme pour le traitement de toute les rougeoles et une troisième dose au bout de 4 semaines).

2. Employer un onguent oculaire à base de tétracycline à 1 % 3 fois par jour pendant 7 jours.

3. Utiliser un tampon protecteur pour l'oeil.

Si aucune amélioration n'est notable au bout de trois jours, consulter si possible un agent de santé spécialiste.

NE JAMAIS UTILISER D'ONGUENTS OCULAIRES CONTENANT DES STEROIDES CHEZ LES PATIENTS SOUFFRANT DE ROUGEOLE.

6.7 Antrite

1. Nettoyer les sécrétions des oreilles uniquement avec un coton ou un morceau de linge propre. Ne pas utiliser d'instruments pour nettoyer les oreilles, afin de prévenir les risques de perforation.

2. Administrer des antibiotiques oraux tels que l'amoxycilline ou l'ampicilline.

3. Informer les mères pour qu'elles évitent d'éviter d'employer des remèdes tels que l'application d'huiles, et d'utiliser quelque objet que ce soit pour retirer les sécrétions.

Produits nécessaires contre les complications de la rougeole

Paracétamol	Tab 100 mg
Vitamine A	Caps 200,000 IU, 100,000 IU
Cotrimoxazol	Tab 80 mg
Amoxycilline	Caps 250 mg
SRO (sels réhydratation orale)	Sachet pour un litre
Tétracycline	Onguent oeil 1% tube (5 g)

APPROVISIONNEMENT EN VITAMINE A
Lignes directrices

Il est essentiel d'entretenir un approvisionnement suffisant et ininterrompu de vitamine A jusqu'au point de distribution. Nombreux sont les programmes qui ont souffert d'une mauvaise distribution des compléments vitaminiques à cause d'une planification insuffisante et d'une sous-estimation des délais d'approvisionnement.

Types de préparation

Deux types de préparation de vitamine A se prêtent au traitement de la rougeole :

- **Capsules de gélatine contenant un concentré liquide de vitamine A.** La préparation la plus couramment utilisée est la capsule de 200 000 IU, qui contient en outre 40 IU de vitamine E pour donner une plus grande stabilité et capacité d'absorption. Dans le cas des jeunes enfants qui ne peuvent pas avaler de capsule, la capsule est perforée et vidée de son contenu directement dans la bouche du sujet. Le nombre de gouttes dans chaque capsule varie de 6 à 8. Chaque fois qu'un nouveau lot de capsules est ouvert, il convient de compter le nombre de gouttes en ouvrant une capsule. Le contenu de chaque capsule équivaut à une dose de 200 000 IU. Pour réduire la dose de 200 000 à 100 000 IU (dans le cas des enfants de 6 à 11 mois) on ouvre la capsule et on la vide de la moitié de son contenu, les gouttes restantes étant directement administrées à l'enfant. Les capsules de 200 000 IU sont généralement disponibles dans des flacons contenant 100 ou 500 unités; le coût par capsule revient à quelque 2 cents E.U. Les flacons de 100 capsules peuvent être particulièrement utiles dans les postes de santé périphériques car autrement les produits perdraient de leur effet si les flacons restaient ouverts trop longtemps.

- **Flacon distributeur contenant un liquide ou un sirop.** Il s'agit là d'une solution de rechange mise au point par l'OMS et par l'UNICEF. Elle permet d'injecter directement dans la bouche de l'enfant une quantité précalibrée de concentré. Le principal avantage de cette formule tient à ce qu'elle permet d'administrer les doses de 100 000 IU avec plus de précision et de façon plus propre et plus rapide. Il est en outre fort probable que cette solution soit plus économique.

Les préparations directement disponibles sur le marché, telles que les compléments vitaminiques distribués par le biais des services sanitaires ou vendus dans le commerce dans la plupart des pays sont insuffisantes pour le traitement de la rougeole.

Sources

L'UNICEF est le principal fournisseur de compléments vitaminiques A. Outre les capsules de 200 000 IU, l'UNICEF peut également fournir des capsules contenant, par exemple, 50 000 ou 100 000 IU.

L'UNICEF offre souvent des compléments vitaminiques A dans le cadre de programmes de coopération sanitaire avec différents pays, parfois comme élément d'un ensemble de médicaments essentiels. En l'absence de ce type d'accord, il peut, pour un coût modeste, fournir des compléments vitaminiques A aux autorités d'un pays ou à des organismes publics. Il faut normalement prévoir de 6 à 9 mois pour la livraison. Toutefois, en cas d'urgence, les produits peuvent être livrés en quelques jours. Les organismes publics souhaitant être fournis en vitamine A sont invités à se mettre en rapport avec la représentation de l'UNICEF dans la capitale de leur pays.

De la vitamine A a également été livrée gratuitement à titre expérimental et dans le cadre d'opérations de secours par Task Force Sight and Life, organisation à but non lucratif financée par Hoffman Laroche et basée à Bâle.

Estimation des besoins

Pour mener à bonne fin des opérations de distribution de compléments vitaminiques A, il faut disposer d'une source d'approvisionnement fiable pour que les agents de santé recevant les premiers les cas de rougeole (foyer, communauté, dispensaires ou hôpitaux) puissent administrer les compléments. En suivant les étapes décrites ci-dessous, on peut estimer un stock d'un an. Bien que le nombre de cas est estimé par rapport à la cohorte de naissances, il est clair que tous les cas ne se produiront pas durant la première année de vie.

Première étape

Estimer le nombre de cas de rougeole allant être pris en charge par le centre de santé, ou dans la région couverte par le programme sur une période de 12 mois. Si ces informations ne sont pas disponibles dans les registres des hôpitaux ou des dispensaires, passer à la deuxième étape. Si ces informations sont disponibles, passer à la troisième étape.

Deuxième étape

S'il n'existe pas de données permettant d'estimer le nombre de cas de rougeole, on peut supposer que les enfants de la cohorte de naissances (0 à 11 mois) représentent 4 % de la population totale. S'il n'y a pas de vaccination contre la rougeole dans la région, le nombre escompté de cas de rougeole est celui de la totalité de ces enfants. Pour déterminer le nombre total de cas de rougeole en un an, il convient d'estimer la proportion d'enfants vaccinés, soit la couverture multipliée par un facteur d'efficacité du vaccin de 85 %. On soustrait le résultat obtenu des 4 % de la population totale. En l'absence de données sur la couverture de vaccination, on peut poser l'hypothèse d'une couverture de 60 %. Arrondir à la dizaine la plus proche le résultat final de cas de rougeole escomptés.

Troisième étape

Multiplier le nombre de cas par 2 pour obtenir le nombre de doses à administrer.

Quatrième étape

Etablir une marge pour besoins imprévus (par exemple, épidémie de rougeole ou traitement de cas de xérophtalmie), pertes, réserve de fin d'année et pour tenir compte du fait que les flacons contiennent 100 ou 500 doses.

Cinquième étape

Estimer le nombre de flacons de 100 et 500 capsules nécessaires (voir encadré ci-dessous).

NOTE : Il faut calculer le niveau à partir duquel il faut repasser commande dans le cas des stocks locaux. Dans la mesure du possible, les bons de commande de vitamine A doivent être remplis en temps voulu. La distribution de vitamine A souffre parfois de perturbation intermittentes.

EXEMPLE
Estimation des besoins

1e étape. Population de la région couverte	=	10,000
2e étape. Cohorte de 4 %	=	400
— % d'enfants vaccinés : 60 % x 85 % d'efficacité soit 51 % des jeunes enfants	=	204
— nombre escompté de cas : cohorte moins enfants vaccinés, soit 400-204	=	196
—arrondir	=	200
3e étape.	=	400
4e étape. Nombre de capsules nécessaires par an	= 400 x 1,5 =	600

5e étape. Les besoins s'élèvent à 2 flacons de 500 capsules ou 6 flacons de 100 capsules chacun.

Stockage et entretien des stocks

Les capsules de vitamine A sont généralement conservées dans des flacons opaques pour réduire les effets de la lumière et de la température. Comme la vitamine A doit être protégée contre la lumière du soleil, il ne faut pas placer les capsules dans des récipients transparents. Les préparations de vitamine A sont plus stables que les vaccins et n'ont pas à être réfrigérées. La vitamine A ne doit pas être congelée. La distribution sur le terrain peut se faire simplement une fois par an. Un flacon non entamé peut avoir une durée de vie de deux ans. Chaque flacon doit avoir une date d'expiration. Une fois qu'un récipient est ouvert, il se produit une dégradation progressive et le contenu doit alors être consommé dans les six mois qui suivent l'ouverture dans la mesure du possible. Comme la vitamine A a une durée de vie limitée, les récipients doivent être étiquetés et datés et il est necessaire d'adopter la méthode de gestion des stocks "first in/first out" (premier arrivé, premier utilisé). Les stocks les plus récents doivent être placés derrière les anciens stocks pour faciliter la rotation..

PRISE EN CHARGE DE LA ROUGEOLE

1. Diagnostic de la rougeole
2. Conseils aux mères
3. Dosage de la vitamine A
4. S'informer sur la vaccination
5. Diagnostic des complications
6. Traitement des complications
   - 6.1 Fièvre
   - 6.2 Malnutrition
   - 6.3 Pneumonie
   - 6.4 Croup
   - 6.5 Diarrhée et déshydratation
   - 6.6 Lésions oculaires
   - 6.7 Antrite
   - *Produits nécessaires contre la rougeole*

L'information contenu dans cette section est basé sur le matériel dans les documents qui suivent:

Le Traitement et la Prise en Charge de la Malnutrition Protéine-Energétique Aiguë, Organisation Mondiale de la Santé, Genève, 1981.

Infections Respiratoires Aiguës chez l'Enfant : Traitement dans de Petits Hopitaux dans des Pays en Développement. Manuel Pour Médecins et Agents de Santé, Organisation Mondiale de la Santé, Genève, 1990.

Manuel pour le Traitement de la Diarrheé pour l'emploi des Médecins et Agents de Santé. Organisation Mondiale de la Santé, Genève, 1990.

1. Diagnostic de la rougeole

Il n'y a pas de test rapide de laboratoire pour le diagnostic de la rougeole. On peut poser la définition suivante pour les cas cliniques simples de rougeole :

> **Fièvre pendant plus de trois jours avec une éruption maculo-papulaire caractéristique et au moins l'un des symptômes suivants : toux, nez qui coule, rougissement des yeux.**

Pour établir un diagnostic des complications de rougeole , il faut suivre deux étapes : établir un historique après l'apparition des premiers signes et procéder à un examen clinique conformément à ce qui suit :

Historique

— Questions à poser :

1. Allaitement, et si l'enfant mange des aliments de sevrage.
2. Est-ce que l'enfant peut boire?
3. Toux, respiration rapide et difficile : symptômes de pneumonie.
4. Diarrhée : c'est-à-dire au moins trois selles sans consistance par jour.
5. Sécrétions des yeux ou des oreilles : symptômes de conjonctivite ou d'antrite.
6. Changements dans l'état de conscience : peut être attribuable à la déshydratation ou à l'encéphalite ou peut tout simplement être un symptôme d'un enfant gravement malade.

Examen clinique

—A vérifier en particulier :

1. Température.
2. Poids : si possible, inscrire le poids sur un tableau de croissance. Si le poids a été préalablement relevé, une perte pondérale peut être un signe de déshydratation et de malnutrition.
3. Signes de déshydratation : membranes muqueuses sèches, perte d'élasticité de la peau, instabilité psychomotrice.
4. Taux de respiration et tirage : respiration rapide et tirage sont des signes de pneumonie aiguë.
5. Lésion de la cornée : la partie centrale de l'oeil est normalement claire et noire mais elle peut devenir opaque ou être endommagée.
6. Sécrétion auriculaires : elle ne peut être visible qu'à l'issue d'un examen.
7. La bouche — pour des ulcères.

2. Conseils aux mères

L'enfant sera faible et sujet à infections pendant un certain temps. Dans les cas de rougeole sans complication, la fièvre tombe en l'espace d'une semaine et les éruptions disparaissent au bout de 10 à 14 jours. Cela dit, la vulnérabilité aux maladies et à la mort peut persister pendant un an après la rougeole. On devrait encourager les mères à chercher un traitement dès que possible.

- **Continuer à allaiter** ou donner à l'enfant autant d'aliments de sevrage et de liquides le plus souvent possible. Pendant la période de récupération qui suit la rougeole il importe de lui donner des aliments fortement énergétiques faciles à assimiler, des fruits et légumes "jaunes" ainsi que des légumes verts.

- **Surveiller la fièvre** afin de réduire les risques de convulsion en préservant une température aussi normale que possible.

- **Faire suivre un traitement à l'enfant** si :

  1. Son état général empire.
  2. Sa respiration s'accélère ou devient difficile.
  3. La diarrhée persiste ou des signes de déshydratation apparaissent.
  4. L'enfant ne peut pas boire.
  5. Il commence à avoir mal aux yeux, ces derniers deviennent nébuleux ou sa vision commence à s'altérer.

3. Dosage de la vitamine A

La vitamine A permet de sauver la vie durant les étapes aiguës de la rougeole. Elle réduit en outre la gravité de nombreuses complications à long terme. Il convient d'administrer de la vitamine A à tous les enfants ayant la rougeole :

- Dans les régions où la mortalité attribuable à la rougeole est réputée être élevée.[1]

- Dans les régions qui sont réputées souffrir de carences vitaminiques A.[1]

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1 (NOTE ED. : Toutes les communautés rurales et urbaines à faibles revenus des pays en développement ont beaucoup plus de risques de tomber dans ces catégories. Les études permettant de déterminer la mortalité causée par la rougeole et la prévalence des carences vitaminiques A sont coûteuses et techniquement complexes. Les responsables de programmes de santé primaire doivent eux-mêmes décider s'il est opportun d'investir dans la réalisation de ces études lorsqu'il n'y a pas de données récentes disponibles, ou s'il convient plutôt d'administrer deux doses de vitamine A en supposant que la situation présentée plus haut risque fort de prévaloir dans les communautés en question.)

- Dans n'importe quel cas de rougeole aiguë ou compliquée. Les compléments de vitamine A devraient être administrés aux enfants souffrant de rougeole aiguë même dans les pays industrialisés tels que les Etats-Unis ou les pays d'Europe.

Les compléments de vitamine A sont disponibles en capsules (50 000, 100 000 ou 200 000 IU) ou sous forme de liquide dans un flacon. Il convient de lire les instructions figurant sur les étiquettes avant d'administrer. Dans le cas des enfants de moins de deux ans, il est nécessaire d'ouvrir les capsules. Les capsules présentent cet avantage en ce sens qu'elles peuvent être distribuées aux mères pour qu'elles puissent ensuite les administrer à la maison.

- Administrer directement à l'enfant la première dose de vitamine A.

VITAMINE A EN CAS DE ROUGEOLE

	Dès le diagnostic	Lendemain
Enfants de moins de 12 mois	100,000 IU	100,000 IU
Enfants d'au moins un an	200,000 IU	200,000 IU

- Veiller à ce que la mère comprenne bien les instructions si elle est censée donner la deuxième dose à la maison. S'assurer qu'elle comprend bien qu'il est nécessaire que l'enfant reçoive une seconde dose le lendemain.

4. S'informer sur la vaccination

Poser des questions sur la situation de l'enfant, et des autres enfants au foyer, en matière de vaccination. Chaque contact est une occasion de mettre à jour le carnet de vaccination de l'enfant et de lui administrer des rappels.

5. Diagnostic des complications

Un enfant souffrant de rougeole aiguë ou de complications aura besoin d'un traitement particulier. Dans certains cas, l'enfant devra être orienté en conséquence. On considère que l'enfant souffre de rougeole aiguë ou de complications s'il présente l'un des symptômes énumérés dans l'encadré ci-dessous.

SYMPTOMES	DIAGNOSTIC
Perte de poids récente et considérable	Déshydratation et/ou malnutrition
Toux avec respiration rapide ou Tirage	Pneumonie
Au moins trois selles sans consistance par jour	Diarrhée
Partie centrale de l'oeil opaque	Lésion oculaire avec risque de cécité
Sécrétion auriculaire	Antrite
Convulsions, coma	Encéphalite

6. Traitement des complications

Nombreuses sont les complications qui accompagnent les cas de rougeole aiguë. Les lignes directrices ci-dessous ne prétendent faire face qu'à celles qui sont les plus courantes. On citera notamment la malnutrition, la pneumonie, la diarrhée, les lésions oculaires et l'antrite. Les complications peuvent être complètement traitées. Si elles sont détectées suffisamment tôt, presque tous les enfants peuvent arriver à une pleine récupération.

6.1 Fièvre

1. Le paracétamol est le moyen le plus efficace de combattre la fièvre. En donner à l'enfant lorsqu'il a très chaud ou que sa température (prise à l'aisselle) est de 39°C. Le pacétamol a moins d'effets secondaires que l'aspirine.

2. Lorsque l'enfant a des convulsions attribuables à la fièvre, on peut faire baisser sa température avec des compresses d'eau froide. On peut en outre lui administrer du paracétamol toutes les 4 à 6 heures.

NOTE : la fièvre à elle seule ne justifie pas un traitement aux antibiotiques.

6.2 Malnutrition

Les enfants ayant la rougeole commencent à souffrir de malnutrition pour les raisons suivantes :

- Ils perdent l'appétit à cause de la fièvre et de l'état de malaise général.
- Ils peuvent avoir du mal à manger à cause de douleurs à la bouche.
- L'assimilation des aliments est réduite à cause de la diarrhée.
- La demande en nutriments, quels qu'ils soient, s'accentue durant les phases aiguë et de récupération.
- Il est une erreur fort répandue qui consiste à ne plus donner à manger (au moins) aux enfants qui ont la rougeole.

Les enfants qui souffrent de complications suite à une rougeole doivent **non seulement** prendre suffisamment de liquides **mais également** avoir une ration alimentaire de qualité. Les mesures à prendre face à la malnutrition dépendent du degré de cette dernière et de l'âge de l'enfant. Les lignes directrices suivantes sont recommandées pour les enfants souffrant d'une malnutrition aiguë :

1. Encourager les mères à continuer d'allaiter.
2. Alimenter l'enfant à intervalles réguliers, au moins toutes les deux heures si possible.
3. Dans le cas des nourrissons et des enfants souffrant d'une malnutrition aiguë, commencer par 125 ml de lait moitié dilué par kilogramme de poids. A mesure que l'enfant regagne de l'appétit, la proportion peut être augmentée à 150 ml/kg, et cette fois de lait non dilué.
4. Ajouter de l'huile végétale et du sucre au lait ou aux préparations de sevrage afin d'accroître leur contenu énergétique.

En cas d'hospitalisation, peser l'enfant tous les jours pour suivre ses progrès. Le gain pondéral durant la phase de réhydratation intensive peut être marqué. Après la réhydratation, le "rattrapage" de la croissance devrait continuer d'être très rapide chez les enfants qui ont reçu une alimentation à forte teneur énergétique. Chez les enfants souffrant d'une malnutrition particulièrement grave, l'emploi d'un tube naso-gastrique peut être déterminant pour leur survie.

POUR DE PLUS AMPLES DETAILS VOIR : *Le Traitement et la Prise en Charge de la Malnutrition Protéine-Energétique Aiguë*, Organisation Mondiale de la Santé, Gèneve, 1981.

6.3 Pneumonie

Diagnostic

- La toux et l'accélération de la respiration sont des symptômes de la **pneumonie**. L'enfant doit être calme pour pouvoir écouter sa respiration.

- La toux, l'accélération de la respiration et le tirage sont des symptômes de la **pneumonie aiguë**. Par accélération de la respiration, on entend au moins 50 respirations par minute chez un enfant de 2 à 12 mois et au moins 40 respirations par minute chez un enfant de 12 mois à 5 ans. Le tirage est un net renfoncement de la paroi thoracique apparent entre les côtes, lorsque le sujet aspire.

- Lorsque la **pneumonie est particulièrement aiguë** l'enfant peut être incapable de boire. On peut également détecter une couleur bleutée aux lèvres et à la bouche (cyanose centrale), signe d'un manque d'oxygène dans le sang.

Traitement

1. Traitement de la pneumonie à la maison avec un antibiotique oral tel que le cotrimoxazole, l'amoxyciline ou l'ampicilline.
2. Recommander aux mères de revenir en consultation si la situation s'aggrave et si la respiration devient plus rapide ou difficile.
3. Si la pneumonie est particulièrement grave, hospitaliser si possible pour l'administration d'antibiotiques intramusculaires ou intraveineux.
4. Les enfants souffrant d'une pneumonie aiguë devraient, s'il y en a, recevoir de l'oxygène.
5. Le râle dû à la pneumonie peut également être traité aux antibiotiques. Ne pas employer de bronchodilatateurs tels que le salbutamol. Ne pas employer des stéroïdes pour traiter les râles.

6.4 Croup

Diagnostic

- Le croup se traduit par un bruit rauque lorsque le sujet aspire. Il est causé par une inflammation du larynx, de la trachée ou de l'épiglotte.

- Le croup se caractérise par un bruit particulièrement fort pendant la respiration alors que l'enfant est calme, des signes de tirage et un enrouement. Le danger du croup tient à ce que la respiration peut être gravement obstruée.

Traitement

1. Les cas de croup aiguë sont traités avec des antibiotiques. Employer du chloramphénicol si disponible.

2. Les cas de croup aiguë sont à traiter d'urgence. Administrer immédiatement un antibiotique même si l'enfant va être hospitalisé.

POUR DE PLUS AMPLES DETAILS VOIR : *Infections Respiratoires Aiguës chez l'Enfant : Traitement dans de Petits Hopitaux dans des Pays en Développement. Manuel Pour Médecins et Agents de Santé . Organisation Mondiale de la Santé, Genève, 1990.*

6.5 Diarrhée et déshydratation

Les trois règles du traitement de la diarrhée :

1. Donner à l'enfant plus de liquides que d'habitude afin de prévenir la déshydratation.
2. Faire manger l'enfant avec abondance pour éviter la sous-nutrition. Encourager la mère à continuer d'allaiter.
3. Si l'état de l'enfant ne s'améliore pas au bout de trois jours, ou si l'une des conditions suivantes se produit :

   —augmentation du nombre de selles liquides

   —omissements répétés

   —coif marquée

   —sang dans les selles emmener l'enfant au dispensaire.

Si l'enfant reçoit une solution de réhydratation orale (SRO) à la maison :

- Indiquer à la mère quelles quantités elle doit administrer après chaque selle suspecte et lui donner suffisamment de sachets pour deux jours.
- Montrer à la mère comment mélanger et administrer la SRO.
- Donner une petite cuillerée de SRO toute les 1 à 2 minutes à un enfant de moins de 2 ans et des gorgées fréquentes à un enfant plus âgé.
- Si l'enfant vomit, attendre 10 minutes, puis continuer à lui administrer la SRO, mais plus lentement.

Comment traiter rapidement les cas de déshydratation grave

- **Si vous avez été formé pour administrer des liquides par voie intraveineuse**, commencer immédiatement. Si l'enfant peut boire, lui donner de la SRO par voie orale pendant que le dispositif intraveineux est installé. Vérifier l'état de l'enfant toutes les heures ou toutes les deux heures. Si aucune amélioration n'est apparente accélérer le débit de l'intraveineuse.

- **Si vous ne pouvez pas administrer de liquides par voie intraveineuse**, administrez une solution SRO (20 ml/kg de poids) avec un tube naso-gastrique.

- **Si aucune de ces deux solutions n'est possible**, hospitaliser immédiatement.

En cas de traces de sang dans les selles :

Administrer pendant cinq jours un antibiotique oral recommandé contre les shigella dans votre région.

POUR DE PLUS AMPLES DETAILS VOIR : *Manuel pour le Traitement de la Diarrheé pour l'emploi des Médecins et Agents de Santé . Organisation Mondiale de la Santé, Genève, 1990.*

6.6 Lésions oculaires

Conjonctivite (yeux rouges ou collés) :

Apprendre à la mére à :

1. Nettoyer les yeux de l'enfant avec du coton ou un morceau de linge propre.
2. Administrer un collyre à base de tétracycline trois fois par jour pendant sept jours. La mère devrait :
   - Se laver les mains avant d'appliquer le produit et après avoir terminé.
   - Abaisser la paupière inférieure pour faire apparaître la conjonctive.
   - Placer une faible quantité sur le bord de la conjonctive inférieure.
   - Maintenir l'oeil de l'enfant fermé pendant au moins deux minutes.
3. Eviter d'employer d'autres remèdes.

Lésions de la cornée :

1. Administrer immédiatement des compléments vitaminiques A (deux doses séparées de 24 heures comme pour le traitement de toute les rougeoles et une troisième dose au bout de 4 semaines).

2. Employer un onguent oculaire à base de tétracycline à 1 % 3 fois par jour pendant 7 jours.
3. Utiliser un tampon protecteur pour l'oeil.

Si aucune amélioration n'est notable au bout de trois jours, consulter si possible un agent de santé spécialiste.

NE JAMAIS UTILISER D'ONGUENTS OCULAIRES CONTENANT DES STEROIDES CHEZ LES PATIENTS SOUFFRANT DE ROUGEOLE.

6.7 Antrite

1. Nettoyer les sécrétions des oreilles uniquement avec un coton ou un morceau de linge propre. Ne pas utiliser d'instruments pour nettoyer les oreilles, afin de prévenir les risques de perforation.
2. Administrer des antibiotiques oraux tels que l'amoxycilline ou l'ampicilline.
3. Informer les mères pour qu'elles évitent d'éviter d'employer des remèdes tels que l'application d'huiles, et d'utiliser quelque objet que ce soit pour retirer les sécrétions.

Produits nécessaires contre les complications de la rougeole

Paracétamol	Tab 100 mg
Vitamine A	Caps 200,000 IU, 100,000 IU
Cotrimoxazol	Tab 80 mg
Amoxycilline	Caps 250 mg
SRO (sels réhydratation orale)	Sachet pour un litre
Tétracycline	Onguent oeil 1% tube (5 g)

LES FONDEMENTS SCIENTIFIQUES DE L'UTILISATION DE LA VITAMINE A

Bibliographie et synthèses

Les études ci-dessous montrent que la vitamine A réduit la mortalité attribuable à la rougeole. Initialement, on pensait que cet effet se limitait aux communautés à forte prévalence de carences cliniques de vitamine A (xérophtalmie). Or, les résultats de récentes études, résumés dans la bibliographie ci-dessous, montrent que les avantages des compléments vitaminiques, dans les cas de rougeoles graves ou accompagnés de complications, se font également sentir là où la carence clinique en vitamine A ne constitue pas un problème.

- **Barclay A.J., A. Foster et A. Sommer. 1987. Vitamin A Supplements and Mortality Related to Measles: A Randomized Clinical Trial. Brit Medical J 294:294-296.** Durant des essais cliniques entrepris en Tanzanie durant la saison de la rougeole, 180 enfants de moins de 6 ans hospitalisés avec la rougeole ont été retenus au hasard pour recevoir soit un traitement à base de vitamine A (200 000 IU de vitamine A le jour de l'hospitalisation et une autre dose de 200 000 IU le lendemain) soit le traitement standard sans vitamine A. Le taux de mortalité dans le groupe ayant reçu le complément vitaminique était de 6/88 (soit 7 %) et celle dans le groupe témoin était de 12/92 (soit 13 %). La différence était particulièrement prononcée chez les enfants de moins de 2 ans et ceux souffrant de maladies pulmonaires. L'incidence de la mortalité était plusieurs fois supérieure chez les enfants mal nourris que chez les enfants bien nourris. Les compléments vitaminiques A ont réduit la mortalité dans tous les groupes nutritionnels.

- **Coutsoudis, A., M. Broughton et H.M. Coovadia. 1991. Vitamin A Supplementation Reduces Measles Morbidity in Young African Children: A Randomized, Placebo-Controlled, Double-Blind Trial. Amer J Clin Nutr 54:890-895.** A Durban, en Afrique du Sud, 60 jeunes enfants âgés de 4 à 24 mois (âge moyen 10 à 12 mois) souffrant de rougeole avec complications ont été retenus de façon aléatoire pour recevoir un traitement à base de vitamine A ou un placebo au moment de leur hospitalisation. Le suivi des enfants a été quotidien pendant 8 jours à l'hôpital, puis au bout de 6 semaines et de 6 mois. Les enfants de plus de 12 mois ont reçu une dose de 200 000 IU les 1e, 2e et 8e jours et au bout de 6 semaines après leur hospitalisation. Les enfants plus jeunes ont reçu 100 000 IU au lieu de 200 000. Les résultats ont révélé une réduction sensible de la durée de la pneumonie dans le groupe ayant reçu le complément, ainsi qu'une récupération clinique complète au bout de 8 jours dans 96 % des cas traités à la vitamine A, par opposition à 65 % dans le groupe témoin.

- **Foster, A. et A. Sommer. 1987. Corneal Ulceration, Measles, and Childhood Blindness in Tanzania. Brit J Ophthalmol 71:331-343.** Cent trente enfants de moins de 11 ans souffrant d'ulcères de la cornée ont été soumis à un examen clinique afin de déterminer la cause de l'ulcération. Parmi ces enfants, 40 % avaient moins de 2 ans et 76 % avaient moins de 5 ans. Les mesures de vitamine A sérique ont révélé que 26 % des enfants souffraient de carences vitaminiques A. L'infection rougeoleuse était associée dans 29 % des cas à des ulcères de la cornée chez les enfants de moins de 2 ans, 70 % chez les enfants de 2 à 4 ans et 37 % chez les enfants de 5 à 10 ans.

- **Hussey, G.D. et M. Klein. 1990. A Randomized Controlled Trial of Vitamin A in Children with Severe Measles. The New England J Medicine 323:160-164.** Un essai aléatoire à double aveugle avec placebo administré à un groupe témoin a été entrepris auprès de 189 enfants non exophtalmiques souffrant de rougeole aiguë au Cap, en Afrique du Sud. Deux doses de 200 000 IU chacune ont été administrées au groupe traité à un intervalle d'une journée. Des 12 enfants décédés, 10 avaient reçu un placebo. Les enfants ayant reçu un traitement ont eu une récupération plus rapide de la pneumonie et de la diarrhée, souffraient moins de croup et passaient moins de temps à l'hôpital. Les résultats étaient statistiquement significatifs.

- **Markowitz, L.E., N. Nzilambi, W.J. Driskell et al. 1989. Vitamin A Levels and Mortality Among Hospitalized Measles Patients, Kinshasa, Zaïre. J Trop Pediatrics 35:109-112.** Les niveaux de vitamine A sérique ont été examinés chez 283 enfants de 4 à 60 mois (âge médian 12) hospitalisés avec la rougeole à Kinshasa, Zaïre. Soixante-et-onze enfants sont morts pendant leur hospitalisation. Les enfants de moins de 24 mois avec des niveaux de vitamine A de moins de 5 ug/dl présentaient un risque nette ment supérieur de mortalité que les enfants avec des niveaux supérieurs.

- **Reddy V., P. Bhaskaram., N. Raghuramulu et al. 1986. Relationship between Measles, Malnutrition, and Blindness: A Prospective Study in Indian Children. Amer J Clin Nutr 44:924-930.** Dans le cadre d'une étude prospective de 1 544 enfants de moins de 5 ans provenant de bidonvilles à Hyderabad, Inde, le poids et la taille des enfants a été relevé comme point de repère et les taux de morbidité ont été relevés chaque semaine sur une période de 15 mois. Au total, 318 cas de rougeole ont été recensés, dont 281 suivis pendant une période de 6 mois après la récupération. On a observé des lésions cornéennes dans 3 % des cas de rougeole. Les niveaux de vitamine A sérique étaient nettement réduits chez les enfants souffrant de rougeole. Près de 60 % des enfants ont contracté une broncho-pneumonie ou la diarrhée pendant les phases aiguës de la rougeole et au-delà de trois fois plus d'enfants avec la rougeole ont commencé à souffrir de malnutrition que les enfants sans rougeole présentant une correspondance entre leur âge et leur poids.

Analyse

De récents travaux de recherche ont montré que la vitamine A, non seulement prévient la cécité, mais contribue en outre à prévenir la mortalité infantile et juvénile. Les membranes de l'organisme (tout particulièrement les parois épithéliales) et le système immunitaire ont besoin de vitamine A pour fonctionner normalement et rester en bon état. Les niveaux de vitamine A dans le sang des enfants souffrant de rougeole sont particulièrement bas. Les causes de ce phénomène ne sont pas connues. L'organisme emmagasine de la vitamine A dans le foie et il semble que la rougeole fasse obstacle au relâchement de ces réserves dans le sang. Lorsque les niveaux de vitamine A sont bas, ces tissus ne peuvent plus protéger l'organisme contre les attaques de microbes de l'environnement. Après ces attaques, la capacité des tissus à se réparer eux-mêmes est également réduite. Il s'ensuit une aggravation des infections, des complications plus graves et un accroissement du risque de mortalité.

Ces études montrent que la vitamine A réduit la mortalité attribuable à la rougeole, non seulement dans les communautés où les signes de carences vitaminiques A sont couramment observés, mais également dans les régions où les carences peuvent être marginales ou sub-cliniques.

Ces études révèlent également ce qui suit :

- la diarrhée ne semblait pas réduire l'efficacité des compléments oraux au point d'en réduire les effets. Les patients souffrant de rougeole et de complications sous forme de diarrhée devraient recevoir la même dose de vitamine A que les autres patients souffrant de rougeole.

- les principaux avantages des compléments vitaminiques A peuvent se produire chez les enfants de moins de 2 ans. Cela dit, on a montré que les avantages des compléments vitaminiques pouvaient se faire sentir jusqu'à l'âge de 6 ans. Par conséquent, tous les cas de complications ou de rougeole aiguë devraient recevoir des compléments vitaminiques A.

- la rougeole présente une étroite relation avec la malnutrition, laquelle prédispose à la mortalité et provient également de la rougeole. En convaincant les mères à accroître activement la ration alimentaire des enfants qui se récupèrent de la rougeole ont peut sauver des vies. Par conséquent, le traitement actif de la rougeole avec des thérapies nutritionnelles - dont l'administration de compléments vitaminiques A pendant les épisodes de rougeole aiguë et l'augmentation des rations alimentaires durant la phase de récupération sont clairement justifiés.

- la rougeole et les carences en vitamine A sont d'importants facteurs dans l'apparition de la cécité chez l'enfant. Chez les patients souffrant de rougeole, le risque d'ulcération de la cornée demeure élevé pendant plusieurs semaines après l'infection. A cela on peut associer les carences en vitamine A, l'infection de l'herpès simplex, l'invasion oculaire du virus de la rougeole et l'utilisation de médicaments traditionnels et préjudiciables pour le traitement des yeux.

Guide pour les programmes de soins de santé primaires

PRISE EN CHARGE DE LA ROUGEOLE ET LA VITAMINE A

Introduction

On peut aisément prévenir la rougeole grâce à la vaccination. En dépit de cela, en 1989, 45 millions d'enfants ont souffert de cette maladie dans les pays en développement : 1,4 millions d'entre eux en sont morts. La mortalité attribuable à la rougeole est principalement le résultat de complications telles que la pneumonie, la diarrhée ou le croup. Il est d'autres complications de la rougeole, telles que la cécité, l'antrite, l'encéphalite et les perturbations de la croissance qui provoquent des incapacités à vie. En Afrique seulement, où la prévalence de la cécité chez les enfants d'âge préscolaire est estimée à 1/1000, on estime que la rougeole est la cause de la moitié des cas de cécité chez l'enfant. L'incidence de la mortalité et de la morbidité (attribuables à d'autres maladies de l'enfance) dans les mois qui suivent l'apparition de la rougeole peut être dix fois supérieure chez les sujets qui ont survécu à la rougeole. Cette incidence plus durable, ne commence à être perçue que maintenant, ce qui signifie que les répercussions néfastes de la maladie sont plus graves qu'on ne le pensait.

Pour l'heure, il n'y a pas de cure ou de traitement spécifique contre la rougeole elle-même. Par conséquent les lignes directrices établies pour lutter contre cette maladie visent essentiellement la prévention et le traitement de ses complications : antibiotiques pour les infections secondaires, antipyrétiques contre la fièvre, réhydratation orale contre la diarrhée et soins ophtalmologiques contre les complications oculaires. Des études récemment réalisées en Afrique montrent que la thérapeutique à base de vitamine A réduit les risques de mortalité et les complications des cas de rougeole aiguë de moitié. Bien que la vitamine A n'ait pas d'effet direct sur le virus de la rougeole, elle prévient ou réduit la gravité des complications, théoriquement grâce à son rôle de protection du système immunitaire et du tissu épithélial. La rougeole réduit le niveau de vitamine A sérique, causant ainsi un état de carence qui n'est pas forcément visible à l'issue d'un examen clinique. On pense que le fonctionnement du revêtement épithélial de l'oeil et des voies respiratoires et gastro-intestinales est perturbé lorsque les niveaux de vitamine A sérique tombent et se maintiennent en dessous de certains niveaux critiques. En effet, le virus de la rougeole et d'autres agents pathogènes envahissent alors ces tissus en causant des lésions oculaires, la diarrhée, la pneumonie, le croup et l'antrite.

La vitamine A peut se révéler fort efficace dans la réduction de la mortalité et des complications attribuables à la rougeole, lorsqu'elle est administrée oralement sous forme de liquide concentré en capsule ou en flacon. Aucun savoir-faire technique, aucun équipement particulier n'est nécessaire. Etant donné que les impératifs techniques et opérationnels du traitement de la rougeole à base de vitamine A sont peu nombreux, ce traitement peut facilement être ajouté aux techniques de lutte déjà en place. Chaque programme devra adapter la composante vitamine A pour qu'elle puisse s'inscrire dans les politiques et pratiques en vigueur. De manière plus précise, les mesures suivantes devraient être prises :

- Publication de lignes directrices nouvelles ou révisées sur le traitement des cas de rougeole.
- Formation du personnel sanitaire (agents de santé, superviseurs, formateurs, responsables) sur les raisons d'être et les modalités du traitement de la rougeole par le biais d'une brève formation sur le tas.
- Acquisition et distribution de stocks, notamment de vitamine A.
- Compléments d'information aux rapports et formulaires existants pour assurer un suivi efficace du traitement des cas de rougeole.

Il convient de souligner que l'administration de vitamine A pour les cas de rougeole ne devrait pas faire oublier l'importance de la vaccination univer-

selle, de l'amélioration de la situation nutritionnelle ou des traitements appropriés des complications de la rougeole. En fait, la principale intervention de lutte efficace et durable contre la rougeole est la vaccination universelle. En préservant un bon état nutritionnel chez les enfants de 6 à 24 mois, on peut assurer une réduction des cas de mortalité attribuables à la rougeole et ***à d'autres maladies courantes de l'enfance***. L'expérience clinique révèle cependant que l'on peut enregistrer une réduction spectaculaire de la mortalité liée à la rougeole si tous les enfants qui souffrent de cette maladie reçoivent des compléments vitaminiques A administrés par voie orale. Les coûts en sont minimes.

Le présent dossier contient certains instruments qui faciliteront l'adoption, dans le cadre de programmes existants, de nouvelles connaissances sur les interventions nutritionnelles — en particulier les compléments vitaminiques A — contre la rougeole. L'on a présupposé que les utilisateurs de ce dossier sont familiarisés avec les lignes directrices de vaccination contre la rougeole et les techniques de traitement de la maladie et de ses complications. C'est pourquoi il porte essentiellement sur des informations nouvelles relatives aux interventions contre la rougeole, et en particulier à l'utilisation de la vitamine A en insistant particulièrement sur l'alimentation.

Le présent dossier contient les éléments suivants :

- **Prise en charge de la rougeole**
  Utile pour les agents de santé à tous les niveaux. Il résume tous les aspects des interventions contre les cas de rougeole, depuis le diagnostic jusqu'au traitement.

- **Prise en charge de la rougeole et la vitamine A : diapositives/copies des diapositives et légendes**
  Contient certaines informations pratiques dont ont besoin les agents de santé et leurs supérieurs hiérarchiques. On y explique comment mettre en oeuvre les nouvelles lignes directrices relatives aux compléments vitaminiques A dans le cadre d'un programme complet de lutte contre la rougeole.

- **Approvisionnement en vitamine A : lignes directrices**
  Utile pour les employés chargés de la commande des fournitures et de la gestion des stocks.

- **Les fondements scientifiques de l'utilisation de la vitamine A : bibliographie**
  Contient des informations techniques pour les médecins, les chercheurs et les responsables dotés d'une formation technique.

Conseillers techniques :

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Moses Chirambo, Représentant Afrique de Sight Savers, Lilongwe
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UN ESTUDIO CONTROLADO, ALEATORIZADO DE VITAMINA A EN NIÑOS CON SARAMPION GRAVE.

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Resumen. *Antecedentes.* **Cerca de dos millones de niños mueren anualmente por sarampión y no existe tratamiento específico para la enfermedad. Se ha sugerido que la vitamina A podría ser beneficiosa en el tratamiento del sarampión.**

Métodos. **Efectuamos un ensayo doble ciego, aleatorizado en 189 niños que fueron hospitalizados en un centro regional de Sudáfrica debido a sarampión complicado con neumonía, diarrea o croup. Los niños (mediana de edad: 10 meses) fueron asignados ya sea a un grupo que recibió vitamina A (dosis oral total de 400,000 UI de palmitato de retinol; n=92) o a un grupo que recibió placebo (n=97) iniciándose en los cinco días después del aparecimiento de la erupción. Las características de ambos grupos eran similares al inicio del estudio.**

Resultados. **Pese a que la deficiencia clínica de vitamina A es rara en esta población, los niveles séricos de retinol de los niños estaban marcadamente deprimidos (promedio [± error estándar], 0.405 ± 0.021 mol/litro [11.6 ± 0.6 g/dl] y 92 por ciento de ellos tenía hiporetinemia (niveles séricos de retinol menores de 0.7 mol/litro (20 g/dl). Las concentraciones séricas de proteína ligadora de retinol (promedio, 30.1 ± 2.0 mg/litro) y albúmina (promedio, 33.4 ± 0.5 g/litro) también se encontraron bajas. Los niños que recibieron vitamina A, comparados con los que recibieron placebo, se recuperaron más rápidamente de neumonía (promedio, 6.3 vs. 12.4 días, respectivamente; p<0.001) y diarrea (promedio, 5.6 vs. 8.5 días; p<0.001), tuvieron menos croup (13 vs. 27 casos; p=0.03) y tuvieron menor tiempo de estancia hospitalaria (promedio, 10.6 vs. 14.8 días; p=0.01). De los 12 niños que fallecieron, 10 eran del grupo placebo (p=0.05). El riesgo de muerte o de complicación seria durante la hospitalización entre los niños tratados con vitamina A fue la mitad de aquél del grupo control (riesgo relativo, 0.51; intervalo de confianza del 95 por ciento, 0.35 a 0.74).**

Conclusiones. **El tratamiento con vitamina A reduce la mortalidad y la morbilidad por sarampión y todos los niños con sarampión grave deberían recibir suplementos de vitamina A, se les demuestre o no una deficiencia nutricional. (N Engl J Med 1990; 323:160-4)**

El sarampión sigue siendo una enfermedad devastadora para la cual no se cuenta con un tratamiento específico. Las esperanzas para su control y su eventual erradicación descansan en la inmunización, pero el sarampión mata cerca de dos millones de niños cada año[1] e invalida a un número desconocido por ceguera[2] y enfermedad pulmonar.[3,4] La idea de que la vitamina A podría tener un efecto protector en el sarampión fue sugerida inicialmente hace más de 50 años[5] pero fue ignorada hasta que Barclay y cols.,[6] en un ensayo clínico aleatorizado, encontraron el doble de fallecimientos en un grupo control (12 de 92) comparado con el grupo de niños que recibieron altas dosis de vitamina A (6 de 88).[6] Aunque los resultados en general no alcanzaron significancia estadística, la vitamina A fue

significativamente protectora en el grupo de menores de dos años de edad.

El que la vitamina A pudiera ser beneficiosa en el sarampión es biológicamente plausible.[7] El sarampión deprime los niveles séricos de vitamina A,[8-11] y la hiporetinemia (nivel de retinol por debajo de 0.7 mol/litro [20 g/dl]) se asocia con aumento de la mortalidad por la enfermedad particularmente en niños menores de dos años de edad.[11] Se sabe que la deficiencia de vitamina A producirá una mayor frecuencia, gravedad o muerte en casi todas las enfermedades infecciosas conocidas.[12] El incremento en la susceptibilidad a las infecciones fue una de las primeras características reconocidas de la deficiencia nutricional de vitamina A,[13] y aún la deficiencia moderada parece estar asociada con mayor riesgo de neumonía, diarrea y muerte en la niñez.[14-17] De acuerdo con Scrimshaw y cols. "no hay una deficiencia nutricional en el reino animal que sea más consistentemente sinérgica con la infección que la deficiencia de vitamina A."[12] Ellos dan una lista de cerca de 50 estudios (incluyendo ocho en humanos) de enfermedades de origen bacteriano, viral o protozoario en las que la deficiencia de vitamina A dió como resultado una mayor frecuencia, gravedad o mortalidad.[12] En efecto, algunas veces se ha llamado a la vitamina A como la vitamina "anti-infecciosa".[18]

Emprendimos este estudio porque el sarampión es un problema que oprime a esta parte del mundo[19] y porque los resultados de Barclay y cols.[6] y la evidencia circunstancial parecían prometedores. Subsecuentemente, tomando en cuenta la misma evidencia, la Organización Mundial de la Salud recomendó la suplementación rutinaria de vitamina A para todos los niños con sarampión en regiones donde la deficiencia de vitamina A fuera un problema reconocido y recomendó que "en países donde la tasa de letalidad por sarampión sea uno por ciento o más sería sensible proporcionar suplementos de vitamina A a todos los niños a quienes se diagnostique sarampión."[20] Un problema con esta recomendación es que en comunidades donde el sarampión representa un grave problema la tasa de mortalidad es, a menudo, desconocida. Otro es que la recomendación se basa en evidencia poco concluyente de solamente dos estudios que centraron su atención en la terapia con vitamina A en sarampión.[5,6] Estas son algunas de las razones por las que en Sudáfrica, y posiblemente en otras partes, todavía no se da suplemento de vitamina A rutinariamente a niños gravemente enfermos de sarampión .

METODOS

Aquellos niños con sarampión agudo que requirieron ingreso hospitalario para el tratamiento de complicaciones asociadas entraron a un estudio controlado, doble ciego, aleatorizado, para evaluar el efecto de la vitamina A sobre la morbilidad y la mortalidad. El estudio se limitó, "a priori", a una fecha fija de finalización, con un reclutamiento máximo de 200 casos; fue realizado de marzo a julio de 1987 en el City Hospital for Infectious Diseases, un centro regional que atiende a una población de cerca de dos millones de habitantes de Ciudad del Cabo y áreas circunvecinas. El protocolo fue aprobado por el comité de investigaciones y ética de la Facultad de Medicina.

Selección de Pacientes y Aleatorización.

Todos los niños menores de 13 años de edad referidos al hospital para ingreso por sarampión fueron elegibles para el estudio. Los criterios de exclusión fueron: tratamiento con vitamina A previo a la hospitalización, xeroftalmia al momento o después del ingreso, erupción de más de cuatro días o falta de consentimiento de los padres.

Los pacientes ingresados al estudio fueron aleatoriamente asignados a recibir ya sea 400,000 UI (120 mg) de vitamina A hidromiscible (palmitato de retinilo; Arovit en gotas, Roche, Basilea, Suiza) o un placebo de apariencia idéntica puestos en jeringas y codificados de acuerdo con una tabla de números aleatorios. La enfermera jefe de sala administraba la mitad de la dosis al momento del ingreso y el resto al día siguiente, ya sea por vía oral o por sonda nasogástrica. Los niños fueron cuidados por el personal regular de la sala. La terapia concurrente incluía oxígeno, líquidos intravenosos y antibióticos cuando estaban indicados, pero no se daban suplementos vitamínicos adicionales. Uno de los investigadores del estudio evaluaba a los pacientes cada día. El código de los tratamientos asignados no fue roto sino hasta que se completó el estudio.

Investigaciones Iniciales.

Al momento de ingresar al estudio se registró el peso y la talla de los niños y se obtuvo una muestra sanguínea venosa. Los pesos y tallas fueron evaluados contra los estándares del NCHS (Centro Nacional de Estadísticas de Salud).[21] Se efectuó determinación de niveles de hemoglobina, conteo de glóbulos blancos (Coulter modelo S5, Coulter Electronics, Hialeah, Fla.), se estimó el diferencial de leucocitos y se guardó el suero a -70°C. Los niveles séricos de proteína total y albúmina fueron medidos por análisis automatizado (Astra-8, Beckman Instruments, Brea, Calif.). Las concentraciones séricas de vitamina A (como retinol) fueron estimadas por cromatografía líquida de alto rendimiento (Dupont Instruments, Wilmington, Del.), con obtención incidental de concentraciones de vitamina E (como α-tocoferol).[22] Se utilizó un integrador programable para cuantificar los resultados cromatográficos (Spectra-Physics, San José, Calif.). Se midió la proteína ligadora de retinol por radioinmunodifusión con un equipo comercial (LC-Partigen, Behringwerke, Marburg, República Federal de Alemania). Se efectuaron radiografías torácicas y otras investigaciones cuando estaban indicadas.

Evaluación de Resultados.

Los resultados fueron evaluados únicamente por criterios clínicos. Las variables utilizadas como resultado fueron fallecimiento y gravedad de la enfermedad medida por duración de estancia hospitalaria; duración de la neumonía o diarrea; incidencia de croup "post-sarampion" o estomatitis herpética; y la necesidad de ser transferido al War Memorial Children's Hospital de la Cruz Roja para tratamiento intensivo. La neumonía se definió como la presencia de taquipnea (frecuencia respiratoria mayor de 40 por minuto) con retracción, crepitaciones, o sibilancias. La diarrea fue definida como la deposición de cuatro

o más evacuaciones líquidas por día. El croup sarampionoso se definió como el croup que estaba presente o se instalaba en el día del ingreso. El croup desarrollado después fue categorizado como croup post-sarampión.

Análisis Estadístico.

Los datos fueron analizados en computadora con el programa Epi-Info (versión 3, USD, Stone Mountain, Ga.). Los datos categóricos[23] (v.gr., número de pacientes por grupo) fueron evaluados por la prueba de Chi-cuadrado, aplicando rutinariamente la corrección de Yates para continuidad,[24] o por la prueba exacta de Fisher cuando el número esperado en una celda era igual o menor que cinco.[24] El intervalo de confianza para los riesgos relativos fue calculado según el método de Greenland y Robins.[25] Los datos contínuos[23] (v.gr., nivel de vitamina) fueron comparados por la prueba de Kruskal-Wallis para datos no paramétricos.[23,24] Todos los valores de P reportados son a dos colas, considerando valores menores de 0.05 como estadísticamente significativos.

RESULTADOS

Exclusión de Pacientes

De 224 pacientes con edades menores de 13 años que fueron ingresados al hospital por sarampión durante el estudio, 35 fueron excluídos. En 12 de estos casos la erupción permaneció por cinco o más días; dos habían recibido vitamina A previamente; no se obtuvo consentimiento para la participación de 18 niños porque no iban acompañados por ninguno de los padres al ingreso y en tres los padres no dieron su consentimiento. De ahí que 189 pacientes ingresaron al estudio. No hubo exclusiones por xeroftalmia ni pérdidas después de haber ingresado al estudio.

Características de Ingreso

En general, el grupo placebo y el grupo tratado fueron comparables (Tablas 1 y 2), excepto que los pacientes en el grupo tratado con vitamina A fueron ingresados cerca de 12 horas antes en términos de duración del rash y tuvieron niveles séricos de proteínas totales y albúmina menores que los del grupo placebo. Dos tercios de los niños fueron 12 meses mayores o menores (mediana, 10 meses; límites de 2 meses a 5 años) y la mayoría fueron varones (58 por ciento). Predominaron los de raza negra (72 por ciento) y los restantes eran de razas mixtas. Cinco pacientes de raza blanca fueron excluídos: en dos casos no se obtuvo consentimiento y tres eran mayores de 13 años. El hospital está abierto para todos. Se piensa que el estado de inmunización y factores socio-económicos contaron para las diferencias raciales que se observaron entre la población de estudio y la población general de 14 años o menos en Ciudad del Cabo (57 por ciento de razas mixtas, 25 por ciento negros, 18 por ciento blancos).[27] No se midió la talla en 11 pacientes.

Tabla 1. Características clinicas de ingreso de 189 niños con sarampión segun tratamiento*

Característica	Numero de pacientes	Placebo (n=97)	Vitamin A (n=92)
Edad (meses)		15.06(8,10,15)	15.89(8,10,17)
< 6	7	3	4
6-12	117	64	53
13-23	37	18	19
≥ 24	28	12	16
Macho/hembra		56/41	53/39
Raza Mixta/negro		29/68	24/68
Peso/edad+	189	81.5 (74, 84, 92)	85.7 (77, 85, 96)
<5° percentil	95	51	44
Talla/edad+	178	96.0 (93, 97, 100)	97.1 (93, 96, 101)
<5° percentil	52	25	27
Peso/talla+	178	89.0 (82, 88, 95)	90.3 (84, 91, 97)
<5° percentil	70	41	29
Erupción (dias)++		1.91 (1, 2, 2)	1.72 (1, 5, 2)
Diarrea	152	75	77
Sin neumonía	30	13	17
Neumonía	146	74	72
Sin diarrea	24	12	12
Neumonía y diarrea	122	62	60
Estomatitis herpética	4	1	3
Croup de Sarampión+++	13	4	9

* Valores entre italicos representan promedios, los en paréntesis por 25o percentil, mediano y 75° percentil. Otros valores refieren a numeros de pacientes.

\+ Presentado como porcentaje de 50 percentil de los estandares del Centro Nacional de Estadisticas de Salud.

++ $P < 0.05$ entre tratamientos

+++ Numero de pacientes con croup de sarmpión de severidad necesitando intervención en vías aéreas.

Tabla 2. Valores Inciciales de Sangre y Suero, según Tratamiento

Característica*	Numero de pacientes	Placebo	Vitamin A
		promedio (25°, 50°, 75° percentil)	
Hemoglobina (g/dl)	177	10.73 (10, 10.6, 11.5)	10.78 (10, 10.5, 11.7)
Hematocrito (%)	177	32.4 (30, 32.5, 35)	32.8 (30, 32, 35)
Leucocitos (x 10^9/litro)	117	8.63 (6.3, 7.7, 10.2)	8.99 (6.2, 8.15, 10.25)
Limfocitos (x 10^9/litro)	117	3.39 (2, 3.1, 4.2)	3.42 (1.8, 2.9, 4.3)
Proteina total (g/litro)+	155	58.54 (55, 57, 62)	53.94 (51, 54, 58)
Alibúmina (g/litro)		34.5 (32, 34, 37)	32.4 (29, 33, 35)
Proteina ligadora de retinol (mg/dl)	156	29.6 (14, 18, 30)	30.48 (14, 17, 37)
Vitamina A (retinol)(ug/dl)	156	12.19 (7.7, 10.7, 14.4)	10.95 (6.7, 9.5, 12.6)
Edad < 2 años	131	12.84 (11.4, 15.1, 46.5)	11.1 (6.7, 9.5, 12.4)
Edad ≥ 2 años++	25	8.38 (7.1, 8.1, 10.5)	10.29 (6.4, 10.5, 13.6)
Hiporetinemia	143	68+++	75+++
Vitamina E (mg/litro)		7.94 (5.5, 7.8, 9.4)	6.84 (4.7, 6.8, 8.8)

* Valores de referencia para las característics presentadas son[26]: hemoglobina, 11.5 a 15.5 g por dl; hematocrito 35 a 45 por ciento; leucocitos, 6 a 17x^9 celluas/l; proteina total, 62 a 80 g/l; albúmina, 35 a 50 g/l; proteina ligador de retinol, 22 a 45 mg/l; vitamina A como retinol, 30 a 80 ug/dl; vitamina E como alfa-tocoferol, 5.0 a 20.0 mg/l. No se presentan valores por limfocitos por el razón de varíación considerable según edad.

\+ $P < 0.05$ para comparación entre grupos.

++ Adentro del grupo placebo, el nivel de retinol fué notablemente más bajo en niños ≥ 2 años de edad que en niños < 2 años de edad ($P = 0.026$).

+++ Indica el numero de casos de hiporetinemia (concentración de retinol sérico < 0.7 u mol/l [20ug/dl]).

El peso para edad estaba por debajo del 5° percentil en 52 niños (29 por ciento) - prevalencia similar a la población de referencia local.[28] El peso para edad (por debajo del 5° percentil en 50 por ciento) y el peso para talla (debajo del 5° percentil en 39 por ciento) fue considerado como reflejo de las pérdidas a corto plazo por sarampión[29,30] más que una desnutrición proteico-energética pre-existente, dado que ésta ocurre en uno por ciento o

menos de la población local de referencia.[28] La indicación de hospitalización fue generalmente una combinación de neumonía y diarrea (64 por ciento). La diarrea (64 por ciento), la neumonía (13 por ciento), o el croup sarampionoso (7 por ciento) como único síntoma fueron el motivo de ingreso en los otros casos.

No se obtuvo muestra sanguínea de 15 pacientes, y en otros 19 solamente se obtuvieron resultados parciales (Tabla 2). Los niveles séricos fueron bajos para proteínas totales (promedio [± error estándar], 56.2 ± 0.7 gramos por litro), albúmina (promedio, 33.4 ± 0.46 gramos por litro), proteína ligadora de retinol (promedio, 30.1 ± 2.02 mg por litro) y vitamina A como retinol (promedio, 0.405 ± 0.021 μmol/litro [11.6 ± 0.6 μg/dl]). Los niveles bajos de proteínas totales reflejan la depresión de las concentraciones de la albúmina sérica (r^2=72.6 por ciento, $p<0.001$). Los niveles séricos de retinol estaban por debajo de los límites bajos de normalidad (0.7 μmol/litro [20 μg/dl]) en 92 por ciento de los niños (143 de 156) y 46 por ciento (72) tenían niveles por debajo de 0.35 μmol/litro (10 μg/dl), colocándolos a riesgo de xeroftalmia,[31] aunque no se observó ningún caso. Los niveles de vitamina E estaban entre límites normales.

Resultados

Los niños que recibieron vitamina A tuvieron una marcada disminución de mortalidad y morbilidad (Tabla 3), sin que se vieran efectos clínicos adversos. Doce niños fallecieron (6.3 por ciento), de los cuales 10 eran del grupo placebo ($p=0.046$). Los niños fallecidos tenían entre 5 a 29 meses de edad, siete eran varones. La muerte ocurrió entre 3 a 32 días después del ingreso (mediana, 10.5). La neumonía[3,32] causó 10 muertes, los otros dos niños fallecieron después de 15 y 32 días, respectivamente, de sepsis fulminante que siguió a diarrea crónica y kwashiorkor inducido por el sarampión. El croup se presentó como un hallazgo incidental en 5 de 10 niños que fallecieron de neumonía.

La duración de los casos de neumonia fué casi dos veces más en el grupo placebo que en el grupo tratado con vitamina A ($p<0.001$) y el 66 por ciento de los niños con neumonía crónica (mayor de 10 días) estaban en el grupo placebo ($p=0.008$). De manera similar, la diarrea continuó por un período tres veces mayor en el grupo placebo ($p<0.001$) y 72 por ciento de los niños con diarrea crónica estaban en este grupo ($p=0.023$). El croup post-sarampión fue más común en el grupo placebo ($p=0.033$), así como la estomatitis herpética ($p=0.08$). Finalmente, la estancia hospitalaria de los sobrevivientes fue tres veces más corta en el grupo tratado con vitamina A ($p=0.004$).

En general, 77 niños presentaron resultados adversos (Tabla 3), de los cuales 52 estaban en el grupo placebo ($p=0.004$). Comparados con los niños del grupo placebo, los niños tratados con vitamina A tuvieron menores riesgos relativos de muerte (riesgo relativo, 0.21; intervalo de confianza del 95%, 0.05 a 0.94), neumonía prolongada igual o mayor de 10 días (riesgo relativo, 0.44; intervalo de confianza del 95%, 0.24 a 0.80), diarrea prolongada igual o mayor de 10 días (riesgo relativo, 0.44; intervalo de confianza del 95%, 0.19 a 0.86), croup post-sarampión (riesgo relativo, 0.51; intervalo de confianza del 95%, 0.28 a 0.92),

intervención en vías aéreas (riesgo relativo, 0.10; intervalo de confianza del 95%, 0.10 a 1.26), estomatitis herpética (riesgo relativo, 0.38; intervalo de confianza del 95%, 0.05 a 1.06) y necesidad de cuidados intensivos (riesgo relativo, 0.35; intervalo de confianza del 95%, 0.13 a 1.16). El riesgo general de un resultado adverso en los niños tratados con vitamina A fue la mitad del de los niños del grupo placebo (riesgo relativo, 0.51; intervalo de confianza del 95%, 0.35 a 0.74). De los 77 niños que tuvieron resultados adversos, solo dos fueron ≥ 2 años de edad ($p=0.002$ y el riesgo en un niño ≥ 2 años de edad fue sustancialmente menor que en los más pequeños (riesgo relativo, 0.15; intervalo de confianza del 95%, 0.02 a 0.91). Ningún niño con concentración de retinol $\geq$ 0.7 μmol/litro (20 μg/dl) falleció; sin embargo el escaso número de niños en este grupo ($n=14$) deja en duda la significancia de este hallazgo.

Tabla 3. Mortalidad y Morbilidad in 189 niños con sarampión, segun tratamiento*

Característica	Placebo (n=97)	Vitamin A (n=92)	Reisgo Relativo (95% IC)+	Valor P
Fallecimiento	10	2	0.21 (0.05-0.94)	0.046
Edad de muerte (meses)				
< 6	1	0		
6-12	7	1		
13-23	1	1		
≥ 24	1	0		
Neumonía (dias)				
Duración	12.37 (5, 8, 17)	6.53 (3, 5, 8.5)		< 0.001
≥ 10	29	12	0.44 (0.24-0.80)	0.008
Diarrea (dias)				
Duración	8.45 (5, 7, 10)	5.61 (3, 5, 7)		< 0.001
≥ 10	21	8	0.40(0.19-0.86)	0.023
Croup post-sarampión	27	13	0.51 (0.28-0.92)	0.033
con intervención en vias aéreas	9	3	0.35 (0.10-1.26)	0.16
Estomatitis herpética	9	2	0.23 (0.05-1.06)	0.08
Cuidados intensivos	11	4	0.38 (0.13-1.16)	0.13
Resultado adverso++	52	25	0.51(0.35-0.74)	< 0.001
Estancia hospitalaria (dias)+++	15.24 (8, 11, 19)	10.52 (7, 9, 13)		0.004

*Por cada tratamiento los valores en italicos representan promedios, los valores in paréntisis representan 25°, 50° y 75° percentiles. Otros valores refieren a numeros de pacientes.

+Riesgo relativo refiere a la proporción entre cada acontecimiento en el grupo vitamina A comparación con el grupo placebo. IC refiere a intervalo de confidencia.

++Incluye fallecimiento, neumonia ≥ 10 dias de duración, croup post-saramipión, o remisión para cuidado intensivo.

+++Refiere a los niños sobrevivientes.

Discusión

Los resultados de nuestro estudio, controlado, aleatorizado, indican un marcado efecto protector de la vitamina A en el sarampión, no obstante la provisión de cuidados médicos generales y la presencia de enfermedad avanzada y complicada. La vitamina A redujo la tasa de mortalidad a más de la mitad y la duración de neumonía, diarrea y estancia hospitalaria a cerca de un tercio. La incidencia de estomatitis herpética y la necesidad de cuidados intensivos parecen haber sido reducidas por la vitamina A. La consistencia del beneficio respecto a todas las variables resultado es notable, dado que la mortalidad no es un criterio sensible. Los estudios previos sobre sarampión[5,6] carecían de poder estadístico para establecer el beneficio de la vitamina A debido a que se apoyaban en las tasas de mortalidad.

La respuesta favorable al tratamiento con vitamina A puede entenderse en términos de la altísima incidencia (92 por ciento) de hiporetinemia en nuestros pacientes (Tabla 2). La hiporetinemia implica un estado de deficiencia de vitamina A a nivel tisular dado que virtualmente no hay depósitos tisulares periféricos de vitamina A excepto en la retina.[33-36] Niveles séricos de retinol por debajo de 0.7 μmol/litro (20 μg/dl) parecen ser inadecuados para las necesidades biológicas del cuerpo.[33] La vitamina A por vía oral es bien absorbida aún en pacientes con diarrea,[37] de manera que los efectos observados pueden ser razonablemente atribuídos a la corrección del déficit tisular de vitamina A. No sabemos, sin embargo, si la deficiencia fue corregida mediante el incremento en las concentraciones séricas de retinol o por algún otro mecanismo, ya que no medimos los niveles de retinol sérico después del tratamiento.

La hiporetinemia, así como en este estudio, aparece casi invariablemente en niños con sarampión grave,[8-11] y la reducción en los niveles de retinol sérico se asocia con enfermedad crecientemente grave.[11] Como muchos de estos datos provienen de poblaciones donde la deficiencia nutricional de vitamina A es un problema conocido,[8-10] se ha inferido que la hiporetinemia en el sarampión representa el agotamiento de las reservas hepáticas.[6,7,20] Sin embargo, hay otro posible mecanismo alterno. La hiporetinemia puede ocurrir en presencia de reservas hepáticas adecuadas de vitamina A cuando las reservas no son movilizadas lo suficientemente rápido para satisfacer la demanda.[36] Se ha visto lo anterior en fiebre, neumonía, artritis reumatoidea, hepatitis, amigdalitis aguda y fiebre reumática[36]; en desnutrición proteico-energética[38]; y ahora, también en sarampión.[8] De ahí que, la hiporetinemia observada en niños con sarampión grave en Kinshasa, Zaire,[11] y Ciudad del Cabo, donde la deficiencia nutricional de vitamina A es poco común, podría ser debida a movilización inadecuada de reservas hepáticas. Un estudio realizado hace 25 años demostró que la deficiencia de vitamina A es rara en Ciudad del Cabo, aún en niños con desnutrición proteico-energética grave,[38] y parece que sigue siendo rara. En una revisión de las listas de bases de datos computadorizados de los pacientes internos en nuestro hospital pediátrico, que atiende predominantemente a la comunidad poco privilegiada local, encontramos solamente tres casos de deficiencia clínica de vitamina A entre 161,381 niños ingresados en un período de 13 años; no se informa de ningún caso desde 1985.

En vista de la evidencia de que la hiporetinemia puede ocurrir en presencia de reservas hepáticas de vitamina A adecuadas[38] y en poblaciones no conocidas como deficientes en vitamina A,[11] parecería prudente proceder asumiendo que la adecuación nutricional previa no asegura contra el desarrollo de hiporetinemia en sarampión grave. De modo que, a todo niño seriamente afectado con sarampión, se le debería reponer vitamina A a la dosis proporcionada por Barclay y cols.[6] (400,000 UI), que en nuestro estudio probó ser eficaz y segura. La Organización Mundial de la Salud[20] recomienda una dosis menor (100,000 a 200,000 UI), pero aún no ha sido establecida su eficacia en sarampión.

Se puede preguntar sobre el costo-beneficio del tratamiento con vitamina A para todos los niños con sarampión grave. Sin duda, los niños menores de dos años de edad están a mayor riesgo de sufrir consecuencias graves y se benefician más de la vitamina A. Cuando escasean los recursos, debería darse prioridad a tales niños. En nuestro estudio, sin embargo, la mitad de los niños por arriba de dos años de edad estuvieron a riesgo de xeroftalmia por sus niveles de retinol sérico inferiores a 0.35 μmol/litro (10 μg/dl),[31] por lo tanto deberían tener tratamiento profiláctico con vitamina A. De modo que, cuando los recursos lo permiten, todos los niños con sarampión grave deberían recibir vitamina A suplementaria.

Estamos en deuda con muchos colegas por su crítica constructiva; con el Sr. R. Sayed, estadístico del Departamento de Salud Comunitaria de la Universidad de Ciudad del Cabo, por sus consejos en el diseño del estudio y los procedimientos de aleatorización; con la Sra. G. Joubert, del Consejo de Investigación Médica de Sudáfrica, por su ayuda en la recolección de datos y análisis preliminares; con Glaxo (Sudáfrica), por la donación de nuestra computadora; con el personal de enfermería del City Hospital for Infectious Diseases por su invaluable ayuda, así como con el superintendente médico del hospital, Dr. P.J.W. Roux, por las facilidades; con el Sr. A.F. Rodríguez por la búsqueda de bases de datos de pacientes del War Memorial Children's Hospital de la Cruz Roja; con el superintendente médico, Dr. R.O. Simpson. por permitirnos el acceso a las bases de datos; con el McCaul Bell Bequest del Instituto de Salud del Niño de la Universidad de Ciudad del Cabo por el financiamiento para el Profesor H. de V. Heese que proporcinó fondos para las determinaciones de vitaminas y la proteína ligadora de retinol; y con la Sra. Frances Pocock por efectuar estas determinaciones en el laboratorio del Instituto.

Referencias

1. Grant JP. The state of the world's children, 1988. Oxford: Oxford University PRess, 1988;3.

2. Foster A, Sommer A. Childhood blindness from corneal ulceration in Africa: causes, prevention and treatment. Bull World Health Organ 1986; 64:619-23.

3. Warner JO, Marshall WC. Crippling lung diseae after measles and adenovirus infection Br J Dis Chest 1976; 70-89-94.

4. Kaschula RO, Druker J, Kipps A. Late morphologic consequences of measles: a lethal and debilitating lung disease among the poor. Rev Infect Dis 1983; 5:395-404.

5. Ellison JB. Intensive vitamin A therapy in measles. BMJ 132; 2:708-11.

6. Barclay AJG, Foster A, Sommer A. Vitamin A supplements and mortality related to measles: a randomised clinical trial. BMJ 1987; 294:294-6.

7. Vitamin A for Measles. Lancet 1987; 1:1067-8.

8. Reddy V, Bhaskaram P, Raghuramulu N, et al. Relationship between measles, malnutrition and blindness: a prospective study in Indian children, Am J Clin Nutr 1986; 44:924-30.

9. Inua M, Duggan MB, West CE, et al. Postmeasles corneal ulceration in children in northern Nigeria: the role of vitamin A, malnutrition and measles. Ann Trop Paediatr 1983; 3:191-91.

10. Varavithya W, Stoecker B, Chaiyaratana W, Kittikool J. Vitamin A status of Thai children with measles. Trop Geogr Med 1986; 38:359-61.

11. Markowitz LE, Nzilambi N, Driskell WJ, et al. Vitamin A levels and mortality among hospitalized measles patients, Kinshasa, Zaire. J Trop Pediatr 1989, 35: 109-12.

12. Scrimshaw NS, Taylor CE, Gordon, JE. Interations of nutrition and infection. WHO monograph series no. 57. Geneva: World Health Organization, 1968.

13. Lassen HCA. Vitamin A deficiency and resistance against a specific infection preliminary report J HYG (Lond) 1930; 30:300-10.

14. Milton RC, Reddy V, Naidu AN. Mild vitaman A deficiency and childhood morbidity - an Indian experience. Am J Clin Nutr 1987; 46:827-9.

15. Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory disease and diarrhea in children with preexiting mild vitamin A deficiency. Am J Clin Nutr 1984; 40:1090-5.

16. Sommer A, Tarwotjo I, Hussaini G, Susanto D. Increased mortality in children with mild vitamin A deficiency. Lancet 1983; 2:585-8.

17. Sommer A, Tarwotjo I, Djunaedi E, et al. Impact of vitamin A supplementation on childhood mortality: a randomised controlled community trial. Lancet 1986; 1:1169-73.

18. Green HN, Mellanby E. Vitamin A as an anti-infective agent. BMJ 1928; 2:691-6.

19. Reynolds LG, Hussey G, Kettles AN. Continuing scourge of measles S. Afri Med J 1987; 71:611.

20. Expanded programme on immunization: programme for the prevention of blindness nutrition. Joint WHO/UNICEF statement: vitamin A for measles. Wkly Epidemiol Rec 1987 62:133-4.

21. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. Am J Clin Nutr 1979; 32:607-29.

22. Catignani GL, Bieri JG, Simultaneous determination of retinol and alphtocopherol in serum or plasma by liquid chromatography. Clin Chem 1983; 29: 708-12.

23. Rosner B. Fundamentals of biostatistics. 2nd ed. Boston: Duxbury Press 1986.

24. Siegel S. Nonparametric statistics for the behavioral sciences. New York: McGraw-Hill 1956.

25. Greenland, S. Robins JM Estimation of a common effect parameter from sparse follow-up data. Biometrics 1985; 41:55-68.

26. Behrman RE, Vaughn VC III, Nelson WE, Nelson textbook of pediatrics 13th ed. Philadelphia: W.B. Saunders, 1987.

27. Central Statistical Services, Pretoria. Population Census 1985. Report no. 02-85-02. Pretoria, South Africa: Government Printer, 1986.

28. Hugo-Hamman CT, Kibel MA, Michie CA, Yach D. Nutrition status of pre-school children in Cape Town township. S AFr Med J 1987; 72:353-5.

29. Axton JH. Mealses and the state of nutrition. S Afr Med J 1979; 55:125-6.

30. Morley D. Paediatric priorities in the developing world London: Butterworths, 1973; 207-30.

31. Vitamin A deficiency and xerophthalmia: Report of a joint WHO/USAID meeting. WHO Tech Rep Ser 1976 590:1-88.

32. KIpps A, Kaschula RO. Virus pneumonia following measles: a virological and histological study of autopsy material. S Afr Med J 1976; 50:1083-8.

33. Olson JA. Vitamin A retinoids and carotenoids. In: Shils ME, Young VR, eds. Modern nutrition in health and disease. 7th ed. Philadelphia: Lea & Febiger, 1988:292-312.

34. Pitt GA. The assessment of vitamin A status. Proc Nutr Soc 1981; 40:173-8.

35. Olson JA. Metabolism of vitamin A. Biochem Soc Trans 1986; 14:928-30.

36. Barker BM. Vitami A In: Barker BM, Bender DA, eds. Vitamins in medicine. Vol 2 4th ed. London: Heinemann, 1983:211-90.

37. Molla A, Islam A, Molla MA, Mahan F. Change in serum vitamin A concentration after oral dose in children with diarrhea. J Pediatr 1983; 103:1000-2.

38. Konmo T, Hansen JD, Truswell AS, Woodd-Walker R, Becker D. Vitamin A deficiency and protein calorie malnutrition in Cape Town. S Afr Med J 1968; 42:950-5.

Manejo del sarampión y la vitamina A

Una Guía Para Programas de Atención Primaria de Salud

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Una Guía Para Programas de Atención Primaria de Salud

MANEJO DEL SARAMPION Y LA VITAMINA A

Introducción

El sarampión se puede prevenir fácilmente por medio de la vacunación. Sin embargo, en 1989, 45 millones de niños de países en vía de desarrollo tuvieron el sarampión y, de estos, mas de 1,4 millones murieron. Las muertes por el sarampión ocurren principalmente como consecuencia de complicaciones como la neumonía, la diarrea y el crup (laringo-traqueítis). Otras complicaciones del sarampión tales como la ceguera, la otitis media, la encefalitis y el retraso en el crecimiento, dejan como consecuencia lesiones permanentes. En Africa, donde la prevalencia de ceguera es de 1 por 1000, el sarampión causa la mitad de los casos de ceguera infantil. La incidencia de morbilidad y la mortalidad (por otras enfermedades infantiles) en los meses que le siguen a una epidemia de sarampión pueden llegar a ser diez veces más altas entre los sobrevivientes al sarampión. Este impacto a largo plazo solo ahora se está confirmando, e indica que las consecuencias del sarampión son más serias de lo que se había imaginado anteriormente.

Hasta la fecha no existe una cura o tratamiento específico para el sarampión. Así, las normas para el manejo de la enfermedad están dirigidas a la prevención y tratamiento de sus complicaciones: antibióticos para las infecciones secundarias, antipiréticos para la fiebre, terapia de rehidratación oral para la diarrea, y tratamiento de las complicaciones oculares. Estudios recientes en Africa han demostrado que la terapia con vitamina A reduce en un 50% la tasa de mortalidad y las complicaciones severas del sarampión. Aunque la vitamina A no tiene ningún impacto directo sobre el virus que causa el sarampión, previene o disminuye la severidad de las complicaciones de la enfermedad, posiblemente mediante su papel protector del sistema inmunológico y el tejido epitelial. El sarampión disminuye el nivel sérico de vitamina A, causando una deficiencia que a veces no es obvia en el examen clínico. Se cree que el funcionamiento de las superficies epiteliales del ojo y de las vías respiratorias y digestivas se deteriora cuando el nivel sérico de vitamina A disminuye y persiste por debajo de niveles críticos. Esto permite que el virus del sarampión y otros agentes patógenos penetren dichos tejidos epiteliales, causando daños en el ojo, diarrea, neumonía, crup y otitis media.

La vitamina A puede ser efectiva en la reducción de las muertes y complicaciones asociadas con el sarampión, cuando se administra por vía oral en forma líquida concentrada, ya sea en cápsulas o con un frasco dosificador. No se necesita ninguna habilidad técnica o equipo especial para este procedimiento. Puesto que son pocos los requerimientos técnicos y operacionales para el tratamiento del sarampión con vitamina A, su administración se puede incorporar fácilmente al manejo actual de los casos de sarampión. Cada programa de salud necesitará adaptar el componente de vitamina A para ajustarlo a las políticas y prácticas actuales. Específicamente, se deben ejecutar las siguientes acciones:

- Formulación de nuevas normas o guías o revisión de las ya existentes para el manejo del sarampión.

- Capacitación del personal de salud (trabajadores de salud, supervisores, y administradores), mediante sesiones de entrenamiento cortas, sobre "por qué" y "cómo" se hace el manejo de los casos del sarampión.

- Adquisición y distribución de materiales, incluyendo la vitamina A.

- Adición de información específica en los formularios e informes existentes para vigilar la efectividad del manejo de los casos de sarampión.

Se debe enfatizar que la administración de vitamina A en los casos de sarampión no debe disminuir la importancia que se le debe dar a la vacunación universal, al mejoramiento nutricional, y al tratamiento adecuado de las complicaciones del sarampión. De hecho, la vacunación universal es la primera intervención para el control efectivo y sostenido del sarampión. El mantenimiento de un adecuado estado nutricional en los niños pequeños, especialmente entre los 6 y 24 meses de vida, asegurará la reducción de las tasas de mortalidad por sarampión y **otras enfermedades comunes de la niñez.** Sin embargo, hasta hoy, las experiencias clínicas sugieren que se pueden alcanzar reducciones dramáticas a corto plazo en el número de muertes y en la incapacidad asociadas con el sarampión, si a todos los niños que presentan la enfermedad se les administra dosis altas de vitamina A por vía oral. Los costos son mínimos.

Este paquete contiene algunos instrumentos que facilitarán la incorporación de los conocimientos sobre el manejo nutricional del sarampión — especialmente la administración de vitamina A — en los programas existentes. Se supone que los usuarios de este material ya están familiarizados con las guías de vacunación y el manejo de los casos de sarampión y sus complicaciones. Por esta razón, este paquete se concentra especialmente en la nueva información sobre el manejo de los casos, especialmente en la utilización de la vitamina A y la importancia de la alimentación.

Este paquete contiene:

- ***Manejo de los casos de sarampión***
  (Dirigido a trabajadores de salud de todos los niveles, resume todos los aspectos del manejo de los casos de sarampión, desde el diagnóstico hasta el tratamiento.)

- ***Provisiones de vitamina A: Guía***
  (Dirigido al personal responsable de la adquisición de la vitamina A y su almacenamiento.)

- ***Bases científicas para la utilización de la vitamina A: Bibliografía comentada***
  (Contiene información técnica apropiada para médicos, investigadores y administradores de salud con conocimientos técnicos.)

- ***Manejo de los casos de sarampión y la vitamin A: Diapositivas y texto***
  (Contiene información práctica que necesitan los trabajadores de salud y sus supervisores acerca de la implementación de las nuevas normas o guías para la complementación con vitamina A dentro del contexto de un programa comprensivo de control del sarampión.)

MANEJO DE LOS CASOS DE SARAMPION[1]

1. Diagnóstico del sarampión

No hay una prueba rápida de laboratorio para diagnosticar el sarampión. Una definición clínica sencilla para el diagnóstico del sarampión es la siguiente:

> **Fiebre por más de tres días con un brote máculo-papular característico, y por lo menos uno de los siguientes signos: tos, secreción nasal, ojos rojos.**

Para hacer el diagnóstico de complicaciones del sarampión se deben seguir dos pasos: elaborar la historia clínica y practicar el examen clínico, como se describe a continuación:

Elaboración de la Historia Clínica

—Pregunte acerca de:

1. Lactancia materna, y si el niño está recibiendo alimentos de destete.
2. Sed — síntoma de deshidratación.
3. Tos, rapidez o dificultad para respirar — síntomas de pneumonia.
4. Diarrea — se define como tres o más deposiciones líquidas durante un día.
5. Secreción de los ojos u oídos — síntomas de conjuntivitis y otitis media.
6. Cambios de la conciencia — pueden ser causados por deshidratación o encefalitis, o pueden ser síntomas de que el niño está gravemente enfermo.

Examen Clínico

—Revise especialmente:

1. La temperatura.
2. El peso - si es posible registre el peso en una gráfica de crecimiento. En aquellos casos en los que existe información previa sobre el peso, una pérdida de peso puede ser un indicador de deshidratación o de desnutrición.

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1 La información contenida en esta sección está basada en material de los siguientes documentos: *El Tratamiento y Manejo de la Desnutrición Proteínico-Energética Severa.* Organización Mundial de la Salud, Ginebra 1991. *Infecciones respiratorias agudas en los niños: Tratamiento de casos en hospitales pequeños.* Serie PALTEX para ejecutores de programes de salud No. 24. Organización Panamericana de la Salud, OPS/OMS. Washington, DC 1992. *Manejo del paciente con diarrea. Programa Salud Maternoinfantil,* Control de las enfermedades diarreicas. Organizacion Panamericana de la Salud, OPS/OMS. Washington, DC 1991.

3. Signos de deshidratación — sed, sequedad en las membranas mucosas, pérdida de elasicidad en la piel, agitación.

4. Ritmo respiratorio y hundimiento del pecho — la respiración rápida y el hundimiento del pecho son signos de neumonía severa.

5. Examen de los ojos buscando daños en la cornea — la parte central del ojo que es normalmente transparente y oscura puede volverse opaca o estar dañada.

6. Secreción en los oídos — puede ser visible solamente al examen clínico.

7. Mucosa bucal — ulceraciones

2. Consejos a la Madre

El niño va a estar débil y susceptible a las infecciones por algún tiempo. En casos de sarampión sin complicaciones, la fiebre cederá a la semana y el brote desaparecerá entre los 10 a 14 días. Pero el mayor riesgo de enfermedad y muerte se mantendrá por lo menos durante un año después del sarampión. Se debe estimular a las madres a que busquen ayuda temprana para el tratamiento de enfermedades durante este período.

- **Continúe la lactancia materna**, o trate de dar al niño todo lo que pueda comer de alimentos del destete y líquidos a intervalos frecuentes. Es importante alimentar al niño con comidas ricas en calorías que no contengan mucha fibra, además de frutas y hortalizas amarillas y hojas de color verde oscuro, durante la recuperación del sarampión.

- **Controle la fiebre** para reducir el riesgo de convulsiones, manteniendo la temperatura del niño lo más normal posible.

- **Traiga al niño nuevamente a consulta** en caso de que:

  1. Las condiciones generales empeoren.
  2. La respiración se vuelva rápida o difícil.
  3. La diarrea continúe o aparezcan signos de deshidratación.
  4. El niño no pueda pasar líquidos.
  5. Los ojos duelan, se vean nublados o haya cambios en la visión.

3. Administración de la Vitamina A

La administración de la vitamina A en las etapas agudas del sarampión salva vidas. La vitamina A también disminuye la severidad de muchas complicaciones del sarampión a largo plazo. Deben darse complementos de vitamina A a todos los niños con sarampión:

- En áreas en donde la letalidad por sarampión es alta.[2]
- En áreas en donde se sabe que hay deficiencia de vitamina A.[2]
- En cualquier caso de sarampión severo o con complicaciones. Los complementos de vitamina A se deben utilizar en niños con sarampión severo aún en países industrializados, como en los Estados Unidos o en países europeos.

Los complementos de vitamina A están disponibles en cápsulas (50.000 UI, 100.000 UI, o 200.000 UI) o en forma líquida con un dosificador de presión. Revise las instrucciones en la etiqueta antes de utilizarlos. Las cápsulas se deben abrir cuando se van a administrar a niños menores de dos años. Las cápsulas tienen la ventaja de que se les pueden dar a las madres para su administración en el hogar.

- Déle la primera dosis de vitamina A directamente al niño.

PLAN PARA LA ADMINISTRACION DE LA VITAMINA A EN CASOS DE SARAMPION

	Al diagnóstico	Al día siguiente
Niños menores de 12 meses	100.000 IU	100.000 IU
Niños de 12 meses o más	200.000 IU	200.000 IU

- Haga que la madre observe cuidadosamente, si ella tiene que darle la siguiente dosis en casa. Asegúrese de que ella entienda la necesidad de administrar otra dosis al día siguiente.

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2 (Nota editorial: Todas las comunidades rurales y las urbanas de bajos ingresos en los países en vía de desarrollo están a alto riesgo de caer en estas categorías. Los estudios para determinar las tasas de letalidad del sarampión y la prevalencia de deficiencia de vitamina A son costosos y complejos. Los administradores de programas de atención primaria de salud tendrán que tomar sus propias decisiones sobre si es apropiado invertir recursos en dichos estudios cuando no existen datos o más bien comenzar a administrar dos dosis de vitamina A a todos los casos de sarampión, con base en la presunción de que las condiciones de riesgo antes descritas posiblemente existen en sus comunidades.)

4. Preguntas sobre las vacunas

Pregunte sobre el estado de vacunación del niño con sarampión y de otros niños en la familia. Cada contacto es una oportunidad para ponerse al día en la vacunación y para suministrar las dosis de refuerzo.

5. Diagnóstico de las complicaciones

El niño con sarampión severo o con complicaciones necesita tratamiento especial. En algunas circunstancias dichos niños necesitarán ser remitidos a otros lugares. Un niño presenta sarampión severo o complicaciones si durante el examen clínico se observa cualquiera de los síntomas mencionados en el cuadro :

Signos	Diagnóstico
Reciente pérdida severa de peso	Deshidratación y/o desnutrición severa
Tos con respiración rápida o Hundimiento del pecho durante un día	Neumonía
Tres o más deposiciones blandas	Diarrea
Parte negra del ojo opaca o dañada	Lesión ocular con riesgo de ceguera
Secreción del oído	Otitis media
Convulsiones/Coma	Encefalitis

6. Tratamiento de las complicaciones

Hay muchas complicaciones que se asocian con el sarampión severo. Sin embargo, estas pautas se deben seguir en el tratamiento de las complicaciones más comunes, las cuales incluyen la desnutrición, la neumonía, la diarrea, las lesiones oculares, y la otitis media. Un niño que presenta complicaciones del sarampión se puede tratar exitosamente. Cuando se les presta atención temprana, la mayoría de los niños se recuperan.

6.1 Fiebre

1. La administración de paracetamol es la manera más efectiva de reducir la fiebre. Administre el paracetamol cuando el niño esté muy caliente o cuando la temperatura axilar sea de 39ºC o más. El paracetamol tiene menos efectos secundarios que la aspirina.

2. Cuando un niño tiene convulsiones debido a la fiebre alta, la temperatura se puede disminuir rápidamente frotándole el cuerpo con una toalla humedecida en agua fría. Adicionalmente, administre paracetamol cada 4-6 horas.

NOTA: La fiebre por sí sola no es una indicación para tratamiento con antibióticos.

6.2 Desnutrición

Los niños con sarampión se desnutren por las siguientes razones:

- El apetito disminuye por la fiebre y la enfermedad en general.
- La alimentación se puede dificultar por la presencia de lesiones en la boca.
- La absorción de los alimentos disminuye con la diarrea.
- Hay un incremento en la demanda de nutrientes durante las fases aguda y de recuperación.
- Hay la costumbre errónea de suspender la alimentación o disminuirla en los niños que tienen sarampión.

Los niños que presentan complicaciones del sarampión necesitan **tanto** suficientes líquidos **como** una dieta de alta calidad. El manejo de la desnutrición dependerá de su severidad y de la edad del niño. Las siguientes son las recomendaciones que se deben seguir con niños que estén severamente desnutridos:

1. Estimular a las madres para que continúen lactando.
2. Alimentar al niño frecuentemente, por lo menos cada dos horas cuando sea posible.
3. Para infantes y niños con desnutrición severa, comenzar con 125 ml/kg de leche diluida al 50%. A medida que el apetito del niño mejora, incrementar la cantidad hasta 150 ml/kg de leche completa.
4. Agregar aceite vegetal y azúcar a la alimentación láctea o a las mezclas de alimentos del destete, con el fin de aumentar el contenido de calorías.

Si el niño es hospitalizado, pesarlo todos los días para vigilar su progreso. El aumento de peso durante la fase intensiva de rehidratación puede ser muy notable. Después de la rehidratación, el aumento de peso debe ser todavía muy rápido en los niños que reciben un régimen de alimentación alto en calorías. La alimentación por tubo naso-gástrico puede salvarle la vida a los niños que sufren de desnutrición severa.

PARA MAYOR INFORMACION, VER: *El Tratamiento y Manejo de la Desnutrición Proteínico-Energética Severa.* Organización Mundial de la Salud, Ginebra 1991.

6.3 Neumonía

Diagnóstico:

- Los síntomas de la **neumonía** son tos y respiración rápida. El niño debe estar calmado mientras se observa y se escucha su respiración.

- Los síntomas de la **neumonía severa** son tos, respiración rápida y hundimiento del pecho. (Respiración rápida es: 50 o más respiraciones por minuto en un niño de 2 a 12 meses de edad, 40 o mas respiraciones por minuto en un niño de 1 a 5 años de edad. El hundimiento del pecho es: un claro movimiento hacia adentro (tiraje) de la parte inferior de la cavidad del pecho, que se observa entre las costillas durante la inspiración.)

- Cuando la **neumonía es muy severa**, los niños pueden tener dificultad para pasar líquidos. Puede también haber un tono azuloso en los labios y la boca (cianosis central) como consecuencia de la falta de oxígeno en la sangre.

Tratamiento:

1. Trate la neumonía en la casa por medio de un antibiótico oral como cotrimoxazol, amoxicilina, o ampicilina.

2. Aconseje a la madre que traiga al niño nuevamente si la condición se empeora y la respiración se torna más rápida o difícil.

3. Si la neumonía es muy severa, hospitalice al niño, si es posible, para administrar un tratamiento con antibióticos por vía intramuscular o endovenosa.

4. A los niños que presenten neumonía severa se les debe administrar oxígeno siempre que sea posible.

5. La disnea causada por la neumonía también se puede mejorar por medio de los antibióticos. No utilice un broncodilatador como el sambutamol. No utilice esteroides para tratar la disnea asociada con la neumonía.

6.4 Crup (laringo-traqueítis)

Diagnóstico:

- El crup es un ruido fuerte durante la inspiración. Lo causa la inflamación de la laringe, la traquea, o la epiglotis.

- El crup se caracteriza por dicho ruido en un niño que está calmado, hundimiento del pecho y ronquera. El peligro del crup es que puede ocurrir obstrucción severa de la respiración.

Tratamiento:

1. Trate el crup severo con antibióticos. Use cloramfenicol, cuando sea posible.
2. Al crup severo se le considera como una emergencia médica. Siempre administre un antibiótico inmediatamente, aun cuando el niño sea remitido al hospital.

PARA MAYORES DETALLES, VER: *Infecciones respiratorias agudas en los niños: Tratamiento de casos en hospitales pequeños. Serie PALTEX para ejecutores de programes de salud No. 24.* Organización Panamericana de la Salud, OPS/OMS. Washington, DC 1992.

6.5. Diarrea y Deshidratación

Las tres reglas para el tratamiento de la diarrea en el hogar son:

1. Dar al niño más líquidos de lo usual con el fin de prevenir la deshidratación.
2. Alimentar bien al niño para prevenir la desnutrición. Aconsejar a la madre que continúe lactando.
3. Llevar al niño a un servicio de salud si no se mejora a los tres días, o si desarrolla alguno de los siguientes signos:
   - — Incremento en el número de deposiciones
   - — Vómito o diarrea acuosa persistente
   - — Sed intensa
   - — Sangre en las deposiciones

Si se le va a dar al niño la solución de rehidratación oral (SRO) en el hogar:

- Enseñar a la madre cuánta SRO debe darle al niño después de cada deposición y entregarle suficientes paquetes para dos días.
- Enseñar a la madre cómo mezclar y administrar la SRO.
- Administrar una cucharadita de SRO cada 1-2 minutos para un niño menor de 2 años, y sorbos frecuentes en una taza para niños mayores.
- Si el niño vomita, se debe esperar 10 minutos y luego continuar la administración de la SRO a un paso más lento.

Para tratar la deshidratación severa rápidamente:

- **Si Ud. ha sido entrenado(a) en la administración de líquidos por vía endovenosa**, comience inmediatamente. Si el niño puede beber, administre la ORS por vía oral mientras que se prepara

la venoclisis. Re-evalúe cada 1-2 horas. Si no hay mejoría, administre el goteo endovenoso más rápidamente.

- **Si Ud. no puede administrar líquidos por vía endovenosa**, rehidrate con la SRO (20 ml/kg de peso) utilizando un tubo naso-gástrico.

- **Si no es posible rehidratar al niño por vía endovenosa o naso-gástrica,** remítalo inmediatamente.

Cuando se encuentra sangre en la deposición:

Trate durante cinco días con un antibiótico oral para la shigella que se recomiende en su área.

PARA MAYOR INFORMACION, VER: *Manejo del paciente con diarrea. Programa Salud Maternoinfantil, Control de las enfermedades diarreicas.* Organizacion Panamericana de la Salud, OPS/OMS. Washington, DC 1991.

6.6. Lesiones Oculares

Para conjuntivitis (ojos rojos o pegajosos):

Enséñele a la madre a :

1. Limpiar los ojos con algodón o con un pedazo de tela limpio.
2. Usar un ungüento de tetraciclina para el ojo, tres veces al día durante siete días. La madre debe:
   - Lavarse las manos antes y después de aplicar el ungüento.
   - Bajar el párpado inferior del niño para que se pueda ver la conjuntiva.
   - Colocar una pequeña cantidad de la medicina en el tercio inferior externo de la conjuntiva.
   - Mantener el ojo del niño cerrado durante por lo menos dos minutos.
3. Evitar el uso de otros medicamentos.

Para el daño de la conjuntiva:

1. Administrar inmediatamente complementos de vitamina A: dos dosis con intervalos de 24 horas entre cada una, como se hace en todos los casos de sarampión, y una tercera dosis después de cuatro semanas.
2. Usar un ungüento ocular de tetraciclina al 1%, tres veces al día durante siete días.

3. Colocar un parche protector sobre el ojo. Si no hay mejoría después de tres días, remitir el niño a un especialista.

NUNCA UTILICE UNGUENTOS QUE CONTENGAN ESTEROIDES EN PACIENTES QUE TENGAN SARAMPION.

6.7. Otitis Media

1. Limpiar las secreciones de los oídos con un algodón o una tela limpia. No utilizar ningún instrumento para limpiar los oídos, para evitar la perforación.
2. Administrar un antibiótico oral como la amoxicilina o la ampicilina.
3. Aconsejar a la madre que evite la aplicación de aceites u otros remedios y el uso de objetos para remover la secreción.

Algunos materiales basicos para el tratamiento de las complicaciones del sarampión

Paracetamol	Tabletas de 100 mg
Vitamin A	Cápsulas de 200.000 IU, 100.000 IU
Cotrimoxazol	Tabletas de 80 mg
Amoxicilina	Cápsulas de 250 mg
SRO (sales de rehidratación oral)	Paquetes para 1 litro
Tetraciclina al 1%	Ungüento para el ojo, tubos de 5 gr

PROVISIONES DE VITAMINA A

Guia

Es crítico mantener y asegurar un suministro continuo de dosis altas de vitamina A para su administración. Muchos programas sufren de interrupciones en la distribución de los complementos de vitamina A debido a un planeamiento deficiente y a la subestimación del tiempo que transcurre entre la orden de suministro y la entrega de los materiales que se necesitan para mantener activos los sitios de distribución

TIPOS DE PREPARACIONES

Hay dos tipos de preparaciones de vitamina A que son adecuadas en el tratamiento del sarampión:

- **Cápsulas de gelatina que contienen un concentrado líquido de vitamina A.** La preparación comúnmente utilizada es la cápsula de 200.000 UI, que también contiene 40 UI de vitamina E para mejorar la estabilidad y la absorción. Para niños pequeños que no pueden ingerir la cápsula, el trabajador de salud rompe la parte superior de la cápsula y exprime el contenido directamente en la boca del niño. El número de gotas contenidas en una cápsula de vitamina A varía de 6 a 8. Cuando desempaca cada lote de cápsulas, el trabajador de salud debe contar el número de gotas de una cápsula. El contenido total de una cápsula equivale a una dosis de 200.000 UI. Para reducir la dosis a 100.000 UI (para niños entre 6 y 11 meses de edad), se exprime y se descarta la mitad del número de gotas, y la cantidad restante se le administra al niño. Generalmente, las cápsulas de 200.000 UI están disponibles generalmente en envases de 500 y 100 cápsulas, respectivamente, y el costo por cápsula es aproximadamente de 2 centavos de dólar de los Estados Unidos. Los envases que contienen 100 cápsulas son especialmente útiles para las unidades de salud periféricas, debido a la pérdida de potencia que ocurre cuando se destapa el envase.

Un frasco dosificador que contiene un líquido o jarabe. Esta alternativa, que está siendo desarrollada por la OMS y la UNICEF, administra una cantidad pre-calibrada de líquido concentrado directamente en la boca del niño. Las principal ventaja es que el dosificador facilita administrar con mayor exactitud la dosis adecuada de 100.000 UI en forma más rápida y menos complicada. También tiende a ser más barata.

Las preparaciones que se adquieren sin receta médica, tales como los complementos de multivitaminas que se distribuyen en los servicios de salud y en las farmacias de la mayoría de países, son inadecuadas para el tratamiento del sarampión.

FUENTES

UNICEF, es el principal distribuidor de dosis altas de vitamina A. Además de las cápsulas de 200.000 UI, UNICEF provee cápsulas de otros tipos (por ejemplo, 100.000 UI o 50.000 UI).

UNICEF provee con frecuencia los complementos de vitamina A como parte de acuerdos de cooperación con los programas de salud de los países, o a veces como un componente de paquetes de drogas esenciales. Si no existe dicho tipo de acuerdo, o no se puede llegar a un acuerdo, UNICEF puede proveer, a bajo costo, complementos de vitamina A a los gobiernos o instituciones. Se debe esperar un período normal de entrega de 6 a 9 meses, pero en caso de

emergencia se pueden proveer complementos en un período de días. Las instituciones interesadas en obtener complementos de vitamina A deben contactar la oficina local de UNICEF en la capital de cada país. Sight and Life, de Basilea, Suiza, una entidad sin ánimo de lucro fundada por Hoffman-LaRoche tambien ha donado vitamina A para uso experimental y ayuda de emergencia.

ESTIMACION DE LAS NECESIDADES DE VITAMINA A

Un elemento crítico para el éxito de la complementación con vitamina A es el mantenimiento de un suministro constante para su distribución por parte del personal de salud que identifica casos de sarampión en el hogar, la comunidad, el centro o puesto de salud, y el hospital. Mediante los siguientes pasos se pueden estimar las necesidades de vitamina A para un año. Aunque el número esperado de casos se estima con base en el número anual de nacimientos, no todos los casos de sarampión se presentan durante el primer año de vida.

Pimer Paso:

Estime el número de casos de sarampión que deberá atender el servicio o institución de salud, o que pueden ocurrir en el área que cubre el programa, durante un período de doce meses. Si esta información no está disponible en los registros del hospital, centro o puesto de salud, siga el segundo paso. Si la información está disponible, siga el tercer paso.

EJEMPLO
Estimativo de Necesidades

Paso 1. Población total del área	=	10,000
Paso 2. Número de nacimientos (4%)	=	400
—El porcentaje de niños protegidos equivale a la cobertura de immunización del 60% x 85% de eficacia, o sea el 51% se los niños	=	204
—El número de casos que se esperan es igual al total de nacimientos menos los niños protegidos, o sea 400 - 204E	=	196
—Aproxime a	=	200
Paso 3. Número de cápsulas (dos por caso)	=	400
Paso 4. Núumero total de cápsulas que se necesitan en 1 año (incluye 50% extra para desperdicios, etc), o sea:	= 400 x 1,5 =	600

Paso 5. Se necesitan 2 envases de 500 cápsulas, o 6 envases de 100 cápsulas.

Segundo Paso:

Si no existe otra base para estimar el número de casos de sarampión en su área, suponga que el grupo de niños nacidos en un año (niños de 0 a 11 meses de edad) representa el 4 por ciento de la población total. Si no hay vacunación contra el sarampión en el área, el número esperado de casos de sarampión equivale a todos estos niños. Para estimar el número de casos de sarampión durante un año, calcule la proporción de niños inmunizados, la cual equivale a la cobertura de vacunación multiplicada por una eficacia de la vacuna del 85%. Esta cantidad se substrae del 4% de la población total. Si no dispone de datos sobre cobertura, puede suponer que la cobertura es del 60%. Aproxime el número final de casos estimados de sarampión al múltiplo de diez mas cercano.

Tercer Paso:

Multiplique el número de casos por 2 para calcular el número de dosis que se deben administrar.

Cuarto Paso:

Agregue los suministros para uso inesperado (por ejemplo, un aumento inesperado en el número de casos de sarampión, el tratamiento de casos de xeroftalmia), desperdicios, reservas para el fin del año y ajustes debidos a que las cápsulas vienen en envases de 100 o de 500 unidades.

Quinto Paso:

Haga un estimativo del número de envases de 100 o 500 cápsulas que se necesitarán *(ver el cuadro más adelante)*.

NOTA: Se debe estimar la necesidad de nuevos suministros con base en los inventarios locales y hacer oportunamente los pedidos de cápsulas para garantizar reservas adecuadas. La distribución de vitamina A se ve frecuentemente afectada por suministros intermitentes o irregulares.

ALMACENAMIENTO Y CUIDADO DE LOS SUMINISTROS

Las cápsulas de vitamina A generalmente se empacan en envases de vidrio transparente para protegerlas de los efectos de la luz y la temperatura. Debido a la necesidad de proteger a la vitamina A de la luz solar, las cápsulas no se deben transferir a envases transparentes. Las preparaciones con vitamina A son más estables que las vacunas y no requieren refrigeración. La vitamina A no se debe congelar. La distribución a lugares apartados del área rural se puede hacer cada año. La vida útil de las cápsulas en un envase que no se ha abierto es de dos años. Cada envase debe tener una fecha de expiración. Siempre que se abre un envase ocurre degradación gradual de la vitamina, por lo cual en lo posible se debe utilizar dentro de los siguientes 6 meses. Debido a que la vitamina A tiene una vida limitada, los envases se deben rotular con fechas de vencimiento y los suministros se deben utilizar a medida que van llegando. Los suministros nuevos se deben colocar detrás de los anteriores con el fin de facilitar la rotación.

BASES CIENTIFICAS PARA LA UTILIZACION DE LA VITAMINA A

Bibliografía Comentada

Los siguientes estudios muestran que la vitamina A disminuye los casos de mortalidad por sarampión. Anteriormente se pensaba que este efecto solamente ocurría en comunidades con alta prevalencia de deficiencia clínica de vitamina A (xeroftalmia). Sin embargo, los resultados de estudios recientes, resumidos en esta bibliografía, indican que los beneficios de dosis altas de vitamina A en los casos de sarampión severo o con complicaciones se pueden lograr aún en áreas en donde la deficiencia clínica de vitamina A no es un problema.

- **Barclay A.J., A.Foster, and Sommer, 1987. Vitamin A Supplements and Mortality Related to Measels: A Randomized Clinical Trial. *Brit Medical J* 294:294-296.** En un estudio clínico efectuado durante una epidemia de sarampión en Tanzania, 180 niños menores de 6 años que ingresaron al hospital fueron asignados al azar a un grupo de tratamiento con vitamina A (200.000 UI el día del ingreso, y otras 200.000 UI al día siguiente), o a un grupo de manejo tradicional del sarampión sin vitamina A. La mortalidad en el grupo que recibió la vitamina A fue de 6/88 (7%) comparada con 12/92 (13%) en el grupo de control. La diferencia más grande se observó en los niños menores de 2 años y en los que tuvieron complicaciones pulmonares. La tasa de mortalidad fue varias veces mayor en los niños desnutridos que en los bien nutridos. La vitamina A redujo la mortalidad en todos los grupos nutricionales.

- **Coutsoudis, A.,M. Broughton, and H.M. Coovadia, 1991. Vitamin A Supplementation Reduces Measles Morbidity in Young African Children: A Randomized, Placebo-Controlled, Double-Blind Trial. *Amer J Clin Nutr* 54:890-895.** En Durban, Africa del Sur, 60 niños de 4 a 24 meses de edad (edad promedio de 10 a 12 meses) con complicaciones de sarampión se asignaron al azar a un tratamiento con vitamina A o a un placebo, desde su ingreso al hospital. A los niños se les hizo seguimiento diario durante 8 días en el hospital, y después del egreso a las 6 semanas y a los 6 meses. Se administró una dosis oral de 200.000 UI a los niños mayores de 12 meses en cada uno de los días 1, 2 y 8, y 6 meses después de la hospitalización. Los niños menores de 12 meses recibieron 100.000 UI cada vez. Los resultados mostraron una reducción significativa en la duración de la neumonía y una recuperación completa a los 8 días en el 96% del grupo de tratamiento con vitamina A en comparación con el 65% del grupo de control.

- **Coutsoudis, A., M. Broughton, H.H. Coovadia, and P. Kiepiela, 1992. Vitamin A Supplementation Enhances Specific Ig G Antibody Levels and Total Lymphocyte Numbers While Improving Morbidity in Measles. *The Pediatric Infectious Disease Journal* 11 (3): 203-209.** Se investigó el efecto de suplementación con vitamina A sobre factores inmunologicos en niños de Sur Africa (afectados por sarampión entre las edades de 4 y 24 meses), durante una prueba aleatória de doble-ciego. Los dos grupos (grupo placebo n=31 y grupo tratado n=29) tenían las mismas características de base. El grupo que recibío la vitamina A tuvo menor incidencia de complicaciónes durante el sarampión y de morbilidad durante los seis meses posteriores a la enfermedad. En el grupo tratado hubo un incremento significativo del numero total de limfocitos y en el nivel de anticuerpos contra el sarampión ligados a la inmunoglobulina. El interleukin 2 y los valores de complemento en el plasma no se afectaron por el tratamiento con vitamina A. Estos resultados confirman los hallazgos de investigaciones en animales como a las cuales sugieren que los mecanismos de acción de la vitamina A en la reducción de la morbilidad y mortalidad están parcialmente relacionados con el fortalecimiento de funciones inmunitárias especificas.

- **Foster, A. and A. Sommer.1987. Corneal Ulceration, Measles, and Childhood Blindness in Tanzania.*Brit J Ophtalmol* 71:331-343.** Se examinaron ciento treinta niños menores de 11 años que tenían ulceraciones corneales, con el fin de determinar la causa de las ulceraciones. De estos niños, 40% eran menores de 2 años y 76% eran menores de 5 años de edad. Las mediciones de retinol sérico mostraron que el 26% de los niños tenían deficiencia de vitamina A. El sarampión se asoció con el 29% de las úlceras corneales en los niños menores de 2 años, el 70% en los de 2 a 4 años, y el 37% en los de 5 a 10 años.

- **Hussey, G.D. and M.Klein. 1990. A Randomized Controlled Trial of Vitamin A in Children with Severe Measles, *The New England J Medicine* 323:150-164.** En Cape Cod, Africa del Sur, se efectuó un estudio clínico controlado, doble ciego, con asignación al azar a un grupo de tratamiento con vitamina A y a un grupo con placebo, en 189 niños con sarampión severo y sin xeroftalmia. Al grupo de vitamina A se le administraron 2 dosis de 200.000 UI cada una con un intervalo de un día entre cada dosis. En total murieron 12 niños, de los cuales 10 eran del grupo de placebo. Los niños que recibieron la vitamina A se recuperaron más rapidamente de la neumonía y la diarrea, tuvieron menos crup, y permanecieron menos días en el hospital. Las diferencias fueron estadisticamente significativas.

- **Markowitz, L.E.N. Nzilambi, W.J. Driskell, et al. 1989 Vitamin A Levels and Mortality Among Hospitalized Measles Patients, Kinshasa, Zaire. *J Trop Pediatrics* 35:109-112.** En Kinshasa, Zaire, se estudiaron los niveles séricos de vitamina A en 283 niños de 4 a 60 meses de edad (mediana de 12 meses) que fueron hospitalizados por sarampión. Setenta y un niños murieron en el hospital. El riesgo de mortalidad fue significativamente mayor en los niños menores de 24 meses con niveles de vitamina A por debajo de 5 microgramos por 100 ml. que en los que tenían niveles más altos.

- **Reddy V., P. Bhaskaram., N. Raghuramulu et al. 1986. Relationship Between Measles, Malnutrition, and Blindness: A Prospective Study in Indian Children. *Amer J Clin Nutr* 44:924-930.** En un estudio prospectivo de 1.455 niños menores de 5 años efectuado en comunidades marginadas de Hyderabad, India, se efectuaron mediciones de peso y talla, y se recolectaron datos de morbilidad semanalmente durante un período de 15 meses. En total se identificaron 318 casos de sarampión, de los cuales a 281 se les hizo seguimiento durante 6 meses después de la recuperación. Se observaron lesiones de la córnea en el 3% de los casos de sarampión. Casi un 60% de los niños desarrollaron bronconeumonía o diarrea durante el período agudo del sarampión, y un número tres veces mayor de niños con sarampión llegaron a tener desnutrición severa en comparación con niños sin sarampión apareados por edad y peso al comienzo del estudio.

Discusión

Etudios recientes han demostrado que, además de prevenir la ceguera, la vitamina A es un factor importante en la prevención de la mortalidad infantil. Las membranas de recubrimiento del organismo (especialmente las superficies epiteliales) y el sistema inmunológico necesitan la vitamina A para funcionar normalmente y mantener su integridad. Los niveles de vitamina A en la sangre son bajos en los niños con sarampión, por razones que no se conocen bien. El organismo almacena la vitamina A en el hígado y parece que el sarampión interfiere con su liberación desde los depósitos hacia la sangre. Cuando los niveles de vitamina A son bajos, los tejidos epiteliales no pueden continuar protegiendo al organismo en forma efectiva contra los ataques de agentes infecciosos del medio ambiente. Tambén se reduce la capacidad de recuperación de los tejidos después de estos episodios de infección. El resultado es un incremento en la severidad de las infecciones, complicaciones más serias, y un aumento en el riesgo de muerte.

Estos estudios muestran que la vitamina A disminuye la letalidad en los casos de sarampión, no solamente en comunidades en las cuales es frecuente encontrar signos de deficiencia de vitamina A sino también cuando la deficiencia es marginal o subclínica. Estos estudios también indican que:

- La diarrea al parecer no reduce suficientemente la absorción de dosis altas de vitamina A por vía oral para impedir su impacto terapéutico. Los pacientes con sarampión que tienen diarrea deben recibir las mismas dosis de vitamina A que otros pacientes con sarampión.

- El mayor beneficio de la vitamina A puede ocurrir en niños menores de 2 años. Sin embargo, los beneficios de la vitamina A se observaron hasta los 6 años de edad. Por consiguiente, a todos los casos de sarampión severo o con complicaciones se les debe suministrar dosis altas de vitamina A.

- El sarampión está estrechamente relacionado con la desnutrición, la cual aumenta el riesgo de muerte por sarampión, y también ésta aparece como consecuencia del sarampión. La educación a la madre para que ofrezca más alimentos al niño que se está recuperando de sarampión puede ayudar a salvar más vidas. Por lo tanto, está ampliamente justificado el tratamiento nutricional intensivo del sarampión con la administración de vitamina A durante la fase aguda y la alimentación extra durante la recuperación.

- El sarampión y la deficiencia de vitamina A son factores etiológicos importantes en la ceguera infantil. En los pacientes con sarampión, el riesgo de ulceración de la córnea puede mantenerse alto por varias semanas después de la enfermedad. Este riesgo está asociado con deficiencia de vitamina A, herpes simple, invasión de los ojos por el virus del sarampión, y el uso tradicional de medicinas nocivas para el ojo.