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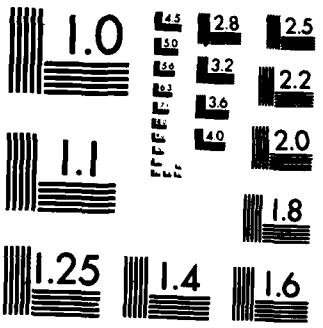
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DEVELOPMENT OF PORTABLE RAPID DIAGNOSTIC MICROBIOLOGY SYSTEMS FOR SUPPORT OF PRIMARY HEALTH CARE DELIVERY

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REPORT NO. 81-32

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Development of Portable Rapid Diagnostic Microbiology Systems for Support of Primary Health Care Delivery *

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* Report Number 81-32, supported by Naval Medical Research and Development Command, Department of the Navy, under Research Work Unit M0095-PN.002-5048. The views presented in this paper are those of the author. No endorsement by the Department of the Navy has been given or should be inferred.

Abstract

Control of infectious diseases in developing countries is essential if social and economic progress is to be made. Accurate, definitive microbiological laboratory data is a prerequisite for infectious disease control. Medical laboratory services must become available to the people, especially children, even though the majority live in rural environments. Rapid microbiological diagnostic systems have been developed and incorporated into portable kits. The kit systems described here offer the potential of providing appropriate technology that can carry the advantages of medical laboratory science to infectious disease patients wherever they may be.

Introduction to the Problem

Infectious diseases cause extensive human suffering and pose major obstacles to both economic and social growth in developing countries. It has been observed that people become poorer because they are sick, and then they become sicker because they are poorer (1). This vicious cycle must be broken for economic development to occur. Advancement of industrialized countries has been positively correlated with improved control of endemic and epidemic infectious diseases (2).

Control of pediatric infectious diseases is especially important. Children represent a vital resource for developing areas; healthy children become strong workers for economic and social advancement while sick, debilitated children become future liabilities for their society. Control of infectious diseases of children should receive primary attention.

In the collective opinion of the delegates to the Alma-Ata Conference in 1978, sponsored by the World Health Organization (W.H.O.) and the United Nations Childrens' Fund (U.N.I.C.E.F.), the key to achieving acceptable levels of health in developing nations lies in primary health care delivery:

"Governments have a responsibility for the health of their people which can be fulfilled only by the provision of adequate health and social measures. A main social target of governments, international organizations and the whole world community in the coming decades should be the attainment by all peoples of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life. Primary health care is the key to attaining this target as part of development in the spirit of social justice"(3).

A prerequisite for adequate infectious disease control and prevention is reliable diagnostic capability. It is necessary to have precise etiologic and epidemiologic information regarding the infectious diseases existing in each geographic area. Frequently, individuals in tropical regions have concomitant diseases, making differential diagnosis difficult, even for most experienced medical practitioners (2). Some acute diseases (typhoid fever and tuberculosis) often mimic other infections. Infections such as cerebrospinal meningitis (CSM) and pneumonia require precise etiologic information for selection of effective therapy. A variety of etiologic agents are common in African CSM outbreaks (4), and appropriate antibacterial therapy for one etiologic agent is not necessarily adequate for another.

These examples illustrate the need for laboratory capability. However, in many developing countries 80% of the people live in rural areas where difficult logistic, communication, and transportation situations exist. Nevertheless, extension of diagnostic laboratory services to these people in their own environments must be accomplished to raise the general level of health.

Rapid, on-site diagnostic capabilities are especially valuable in many children's diseases which are particularly severe and fulminant. Early, correct therapy selected on the basis of precise microbiological data may be the crucial factor for a good prognosis and may also prevent handicapping sequelae that limit the individual's functional place in society. Thus, effective diagnostic microbiology systems, that can define the etiologies of infectious diseases where they are found, are necessary for developing areas.

CONCEPT DEVELOPMENT

Physically bringing medical science to the people in developing countries is difficult. It is primarily a logistic problem. Simplified and portable systems are required. These systems should be appropriate for field work to control epidemics in remote rural areas and also appropriate for routine use in small hospitals and clinics.

The development of a practical approach for streamlining microbiological laboratory diagnostics for the primary health care level required reassessing or even discarding certain conventional concepts. For example, culture isolation and laborious biochemical identification of isolates were methods clearly too complex and expensive to be used in rural settings. On the other hand, certain conventional methods such as microscopy did fulfill requirements for rapid, simple diagnostic methods. Thus, acceptance of some traditional techniques and equipment, modification of others, and application of new technology were all necessary to reach this goal.

Diagnostic microscopy has remained a first-line technique for rapid diagnosis. The approach is straight-forward, and a decision based on direct observation usually can be made immediately. The introduction of new rapidly acting stains and improved differential stains has enhanced the effectiveness of microscopy as a diagnostic tool, and miniaturization of microscopes has improved portability.

Perhaps the most significant recent advances in diagnostic microbiology have been made in sero-diagnostic systems. Improved techniques have been developed to detect and measure antibody, and more importantly, many sero-diagnostic methods are being developed to detect and identify antigens of infecting microorganisms in clinical specimens. Examples of

such methods include enzyme-linked-immunosorbent assay (ELISA), radioimmunoassay (RIA), fluorescent antibody (FA), electrophoretic methods, and inert particle aggregation (IPA) tests. While all these techniques have provided excellent new diagnostic tools, not all are suited to rapid diagnosis in the field or in smaller health facilities. The complex, expensive equipment and special reagents required for RIA, ELISA, and FA make them impractical for use in most developing areas. However, counterimmunoelectrophoresis (CIE), and certain IPA tests - coagglutination (COAG), hemagglutination (HA), and latex agglutination (LA) - offer operational simplicity, rapid results, and economy. Therefore, these appear to be suitable for field-operable rapid diagnostic tests.

PORTABLE KIT EVOLUTION

A portable laboratory kit design has evolved only following the development of a philosophy of rapid diagnostic tests. Both have been based on experience that has indicated which approaches may be appropriate. Two prototype kits have been developed and evolved through actual field experiences and suggestions from working colleagues in developing areas.

The basic kit is a completely portable, self-supporting diagnostic laboratory containing three diagnostic systems (Figure 1). Kit components are housed in a plastic case measuring 47 x 39 x 21 cm. The packed weight is approximately 13 kilograms. Components are protected from shock and temperature extremes by durable plastic foam materials (5).

The small second kit is designed specifically to facilitate diagnostic application of IPA tests. It is included as one of the systems in the basic kit. It may also be employed independently (Figure 2).

The three diagnostic systems in the primary kit are microscopy, CIE, and IPA. These are supplemented by limited selective culture capability for use in certain situations. CIE, COAG, and LA tests, used for both antigen and antibody detection, may be employed for rapid diagnostic methods and for serologic surveys.

Primary equipment in the basic kit includes a McArthur microscope (Figure 3), electrophoresis apparatus (Figure 4), incubator-waterbath, and water purification system. Associated supporting supplies such as electrical adapters, slide reader, slides, stain rack, test tube rack, and work table are all included. There are compartments for storing sero-diagnostic reagents, stains, and CIE reaction slides. Electrical components in the kit operate from 110V or 220VAC mains, from 12VDC automobile batteries, or in some items on flashlight cells.

APPLICATIONS

A wide variety of rapid diagnoses are possible with the three systems in the primary kit. Diagnostic microscopy applications are familiar, blood and stool examination for parasites, Gram-stained smears from lesions and exudates, and darkfield examinations. The CIE test system, detecting both antigens and antibodies, has been used to diagnose a variety of diseases caused by bacteria, fungi, parasites, and viruses. CIE has also found application in other areas such as forensic medicine, snake bite identification, toxin detection, and veterinary medicine. An excellent review of CIE applications has been published by Draper (6). The CIE test system in the kit extends these applications from the laboratory into the field for diagnostic and public health work. The apparatus has simply been miniaturized and has been used to detect both antigens and antibodies in patients with CSM during vaccine field trials in Egypt and the Sudan (7,8). More recently, the kit CIE system was used

to detect and define outbreaks of CSM in Upper Volta. Remote villages were reached by a light plane, and the portable kit was used to determine etiology of the CSM cases. Non-infected children were given specific vaccinations when appropriate (9).

The simplicity of COAG tests recommend them for kit applications. This test utilizes stabilized protein A-containing Staphylococcus aureus cells as carrier particles for specific antisera. COAG reagents are easily prepared, specific, stable, and inexpensive.

The COAG test makes possible a 5 minute bed-side diagnosis of such diseases as CSM and cholera, by testing the primary specimen directly (10). The waterbath-incubator in the kit may be used for enrichment cultures of stool or blood specimens prior to detecting Salmonella antigens with the COAG test (11). Other diagnostic applications require only simple pretreatment of specimens before the COAG test is used; streptococcal pharyngitis identified from throat washings (12) bacterial pneumonia from sputum specimens (13), or typhoid fever from urine specimens (14). The COAG test offers great promise for expanded application.

The small COAG kit (Figure 4) has been used successfully by medical attendants in West African rural clinics to perform rapid, specific diagnoses of CSM cases. The field COAG results were compared with standard bacteriologic techniques at the base laboratory. The correlation of results from 30 CSF specimens obtained in one village was 97%, and was 80% with 20 CSF speciemsn from another village. Small COAG kits supplied with specific reagents for selected endemic diseases appear to be a viable approach to practical microbiologic diagnosis at the primary health care delivery level.

CONCLUSIONS

Prototypes of two portable rapid diagnosis kits have been developed and tested. One is a basic kit containing a variety of test systems; the other is a simple COAG test kit. It has been demonstrated that precise etiologic diagnoses of acute infectious diseases can be made in rural areas of developing countries using these kits and the rapid diagnostic systems they employ. Therapeutic and preventive measures for most infectious diseases are common medical knowledge. When specific diagnoses can be made where the patient is located, then appropriate action can be undertaken immediately. These portable, rapid diagnostic kits represent "appropriate technology" that can provide significant support to primary health care delivery in developing areas. It now remains to confirm their value in a wider variety of situations, with a broader range of infections, and in the hands of other workers (15). Support for final engineering design, production, and distribution is also needed. It is hoped that this kit concept will continue its evolution to provide appropriate laboratory systems to support delivery of health care anywhere in the world.

Legends for figures:

Figure 1: Components of the portable rapid diagnosis kit.

A - Electrophoresis chamber

B - Rinse bottles

C - Staining dip tanks

D - Capillary pipettes

E - Stain bottles

F - Inverter (12 VDC to 110 VAC)

G - Microscope storage

H - Multi-meter

I - Test tube rack and power supply (below)

J - Microscope slides

K - Microscopy supplies

L - Waterbath

M - Work surface

N - Insulation

O - Boiling bath and slide storage

P - Water purifiers

Q - Coagglutination kit

R - Reagent storage

S - Slide viewer

T - Darkfield condenser

U - Flashlight

V - Heater

W - Reagents

X - General supplies (below)

Y - Water bottle

Z - Cups

Figure 2: The coagglutination kit is a compact unit that may be used independently.

Figure 3: The McArthur microscope is a rugged field instrument with full microscopic capabilities.

Figure 4: The compact electrophoresis system operates from 110 VAC, 220 VAC, or 12 VDC electricity sources.

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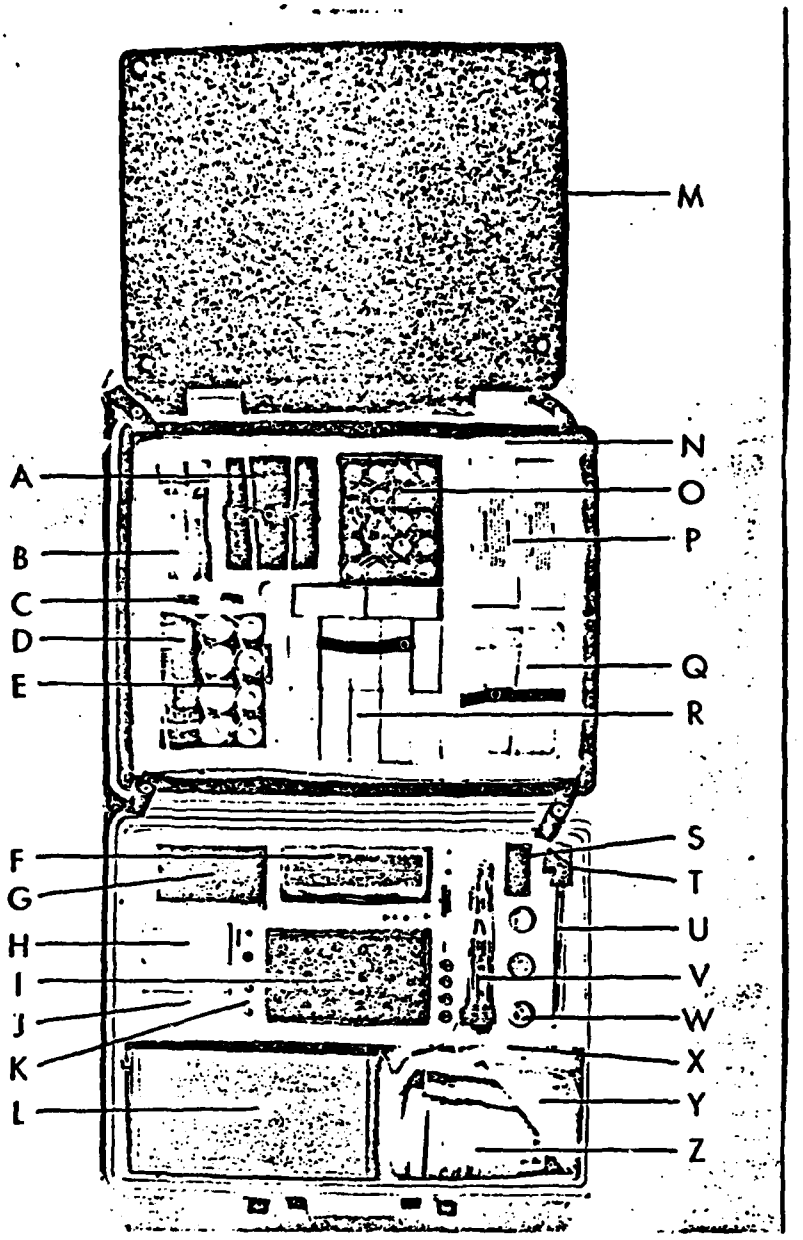
FIGURE 1



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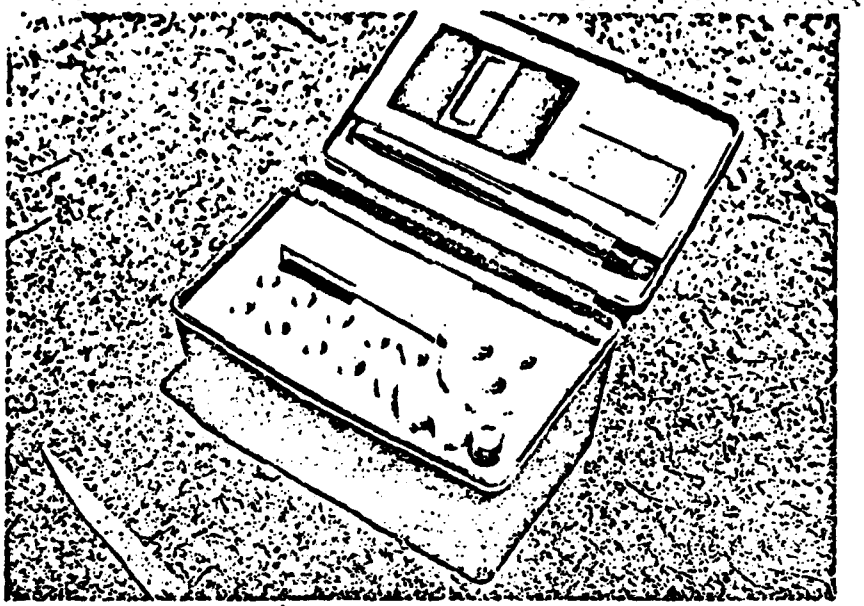

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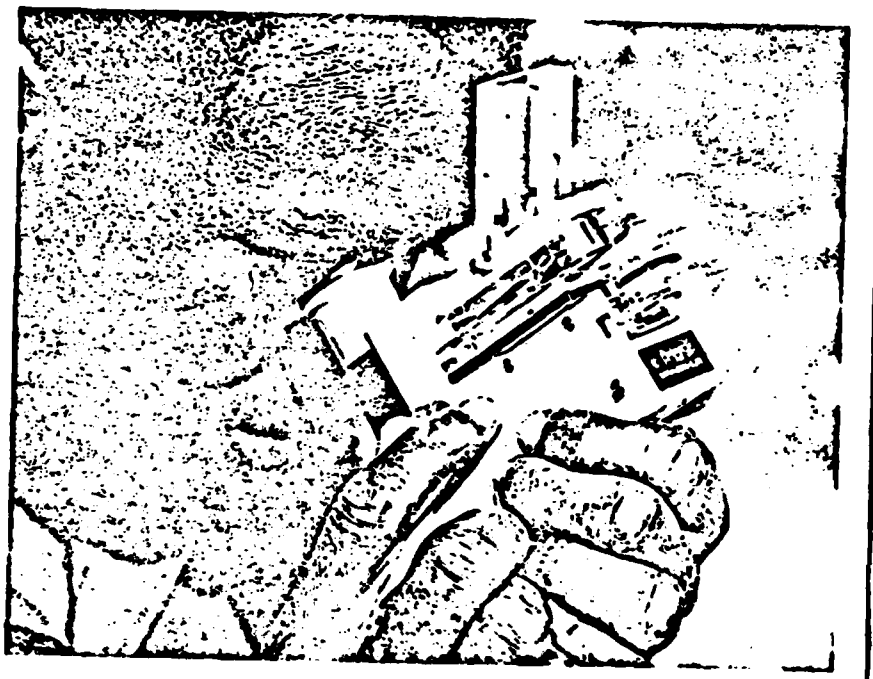
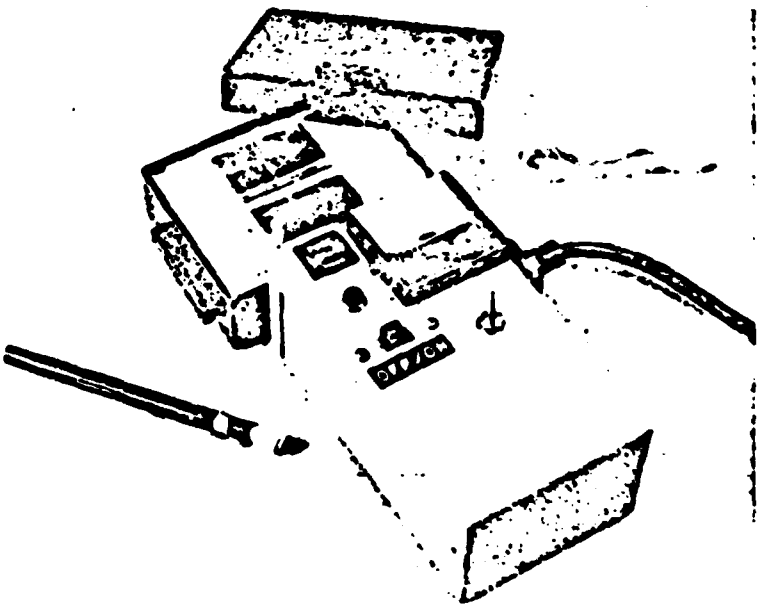


Figure 4



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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 81-32	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) (U) Development of Portable Rapid Diagnostic Microbiology Systems for Support of Primary Health Care Delivery		5. TYPE OF REPORT & PERIOD COVERED Final 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Warren R. Sanborn		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS Naval Health Research Center P. O. Box 85122 San Diego, CA 92138		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS M0095PN.002-5048
11. CONTROLLING OFFICE NAME AND ADDRESS Naval Medical Research & Development Command NMCNCR Bethesda, MD 20814		12. REPORT DATE November 1981 13. NUMBER OF PAGES 13
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office) Commander, Naval Medical Command Department of the Navy Washington, DC 20372		15. SECURITY CLASS. (of this report) UNCLASSIFIED 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

Approved for public release; distribution unlimited.

18. SUPPLEMENTARY NOTES

To be published in: The Indian Journal of Pedicatrics (in press)

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Rapid diagnostic kits
Portable laboratory
Infectious disease
Control

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

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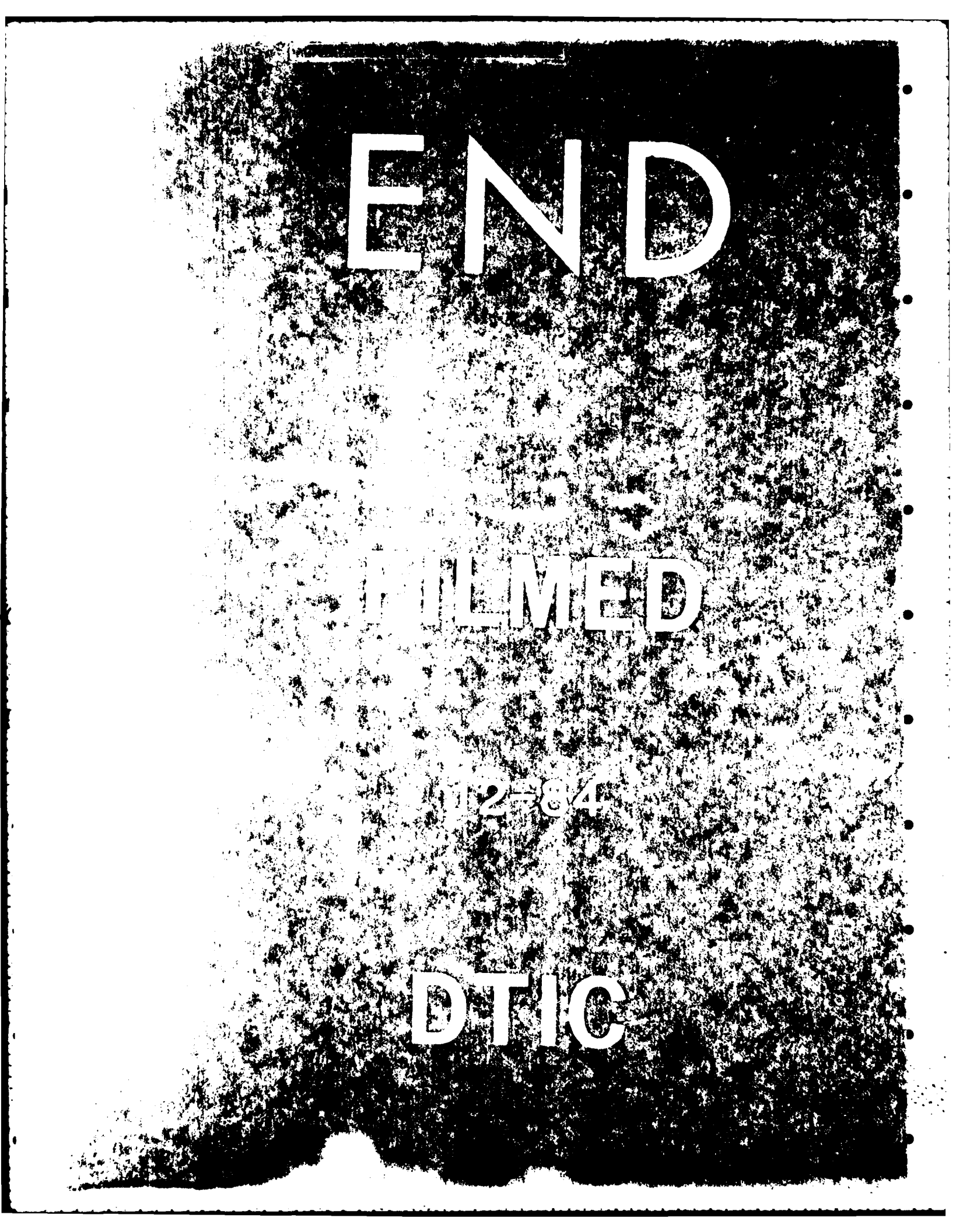
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